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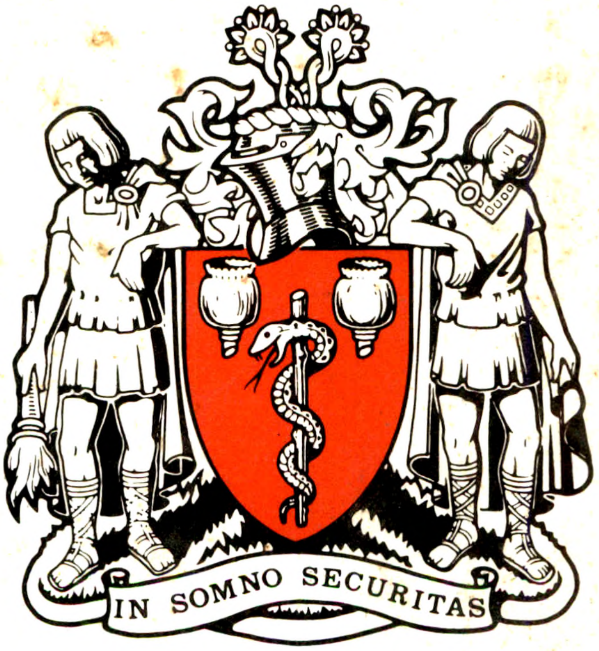

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Prescribing information *Indications and dosage:* Systemic candidiasis: 400mg on the first day followed by 200-400mg once daily. Cryptococcosis, including meningitis: 400mg on the first followed by 200-400mg once daily. Maintenance therapy to prevent relapse of cryptococcal meningitis in patients with AIDS: 100-200mg daily. Oropharyngeal candidiasis: 50-100mg once da 7-14 days or longer in immunocompromised patients. Other mucosal candidal infections: 50-100mg once daily for 14-30 days. Vaginal candidiasis: single 150mg dose. Prevention of fungal inf in neutropenic patients following cytotoxic chemotherapy or radiotherapy: 50-100mg once daily whilst patients are predisposed to such infections. Use in the elderly - as above except for renally impaired - see data sheet. Use in children - not recommended. *Administration:* Diflucan may be administered either orally or by intravenous infusion at a rate of approximately 5-10ml/min. The dosages for the two routes are equivalent. *Contra-indications:* Hypersensitivity to fluconazole or related triazoles, pregnancy and women of childbearing potential unless adequate contraception is employed. *Warnings:* Lactation - not recommended. Renal impairment: dosage reduction may be necessary, see data sheet. *Drug interactions:* Monitor patients on concurrent anticoagulants, oral sulphonylureas, phenytoin or cyclosporin, rifampicin or theophylline. *Side-effects:* Nausea, abdominal discomfort, diarrhoea, flatulence and anaphylaxis. *Package Quantities and Basic NHS cost:* 50mg capsule, calendar pack of 7, £16.61 (PL 57/0289); 200mg capsule, calendar pack of 7, £66.42 (PL 57/0317); 150mg capsule, pack of 1, £7.12 (PL 57/0290); Powder for Oral Suspension, 35ml after reconstitution with water: Bottle of 50mg/5ml, £16.61 (PL 57/0343), Bottle of 200mg/5ml, £66.42 (PL 57/0344); Bottles of 25ml and 100ml containing Diflucan 2mg/ml intravenous infusion - 25ml (50mg) bottle, £7.32; 100ml (200mg) bottle, £29.28 (PL 57/0315). Hospital prices are available on request. *References* 1. Data on file, Pfizer Ltd. 2. Brammer, K.W. (1990), *Haematology and Blood Transfusion*, **33**, 546-550. 3. Samonis, G. *et al.* (1990), *Reviews of Infectious Diseases*, **12**(3), S369-S373. 4. Data on file, Pfizer Ltd. 5. Buxton, M.J. *et al.* (1991), *Journal of Infection*, **23**, 17-31. Further information on request.

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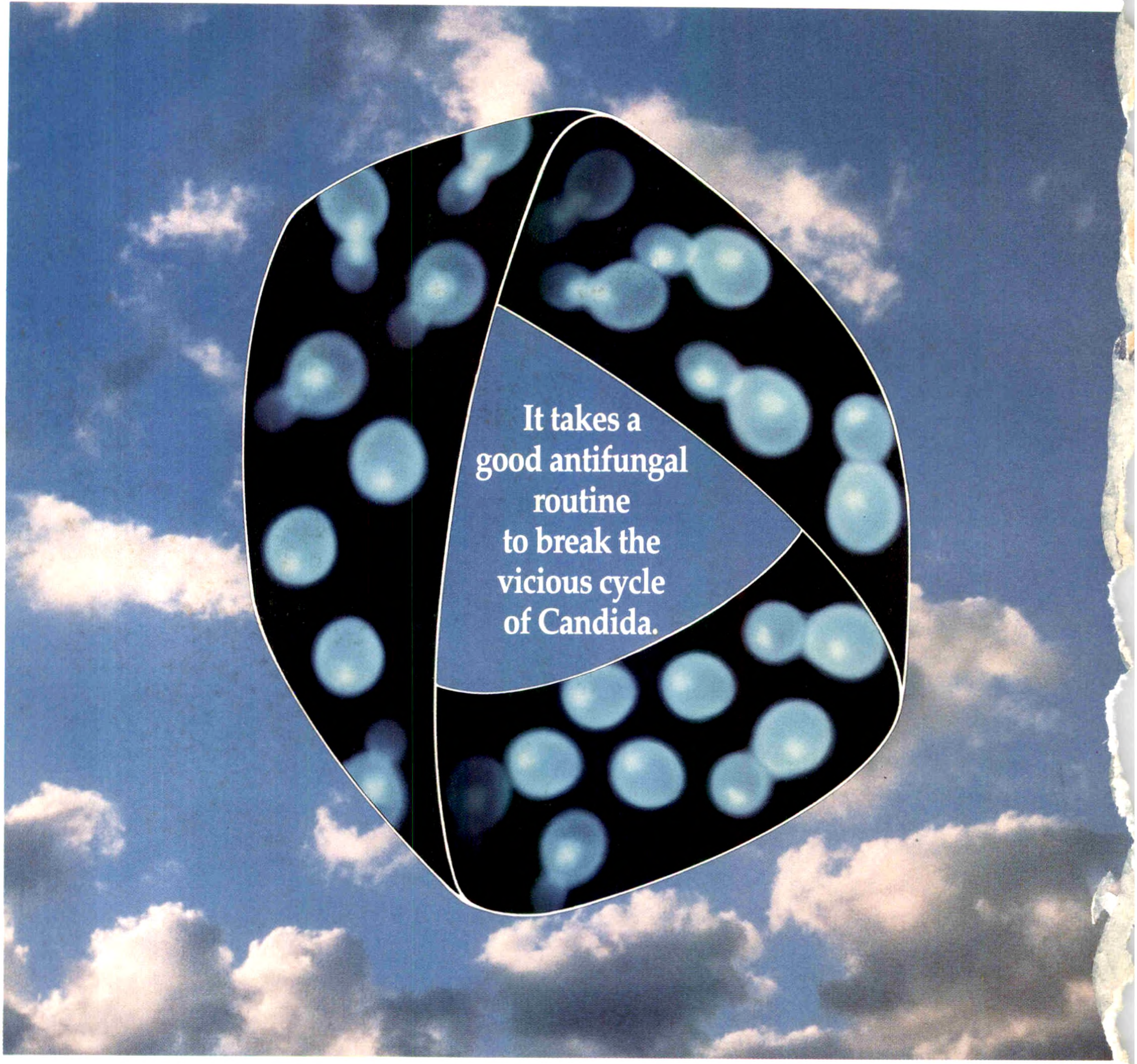

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1. Centres for Disease Control: Increase in national hospital discharge survey rates for septicaemia. *Morbidity and Mortality Weekly Report. 1990;* 39: 31. 2. Kreger, B.E., Craven, D.E., Carling, D.E., McCabe, W.R., *Am. J. Med.*, 1980; 68: 332-344. 3. Straube, R., International Congress for Infectious Diseases. Montreal, Canada. July 15-19, 1990. (Abstract No. 99). 4. Ziegler, F.J., Fisher, C.J. Jr., Sprung, C.L., *et al.*, *N. Engl. J. Med.* 1991; 324: 429-436.

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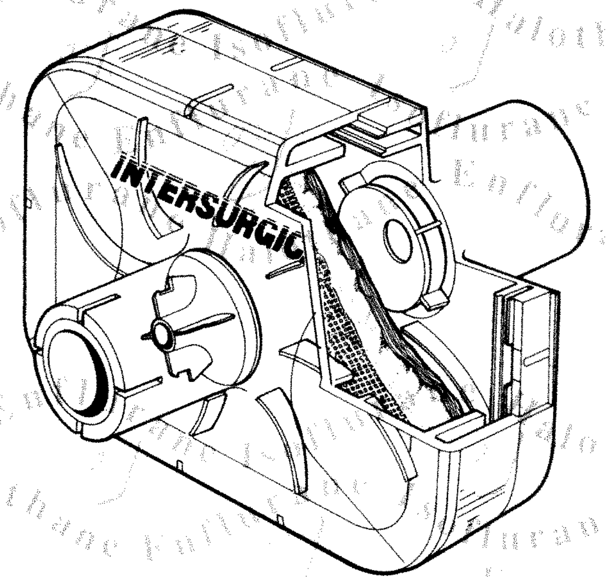

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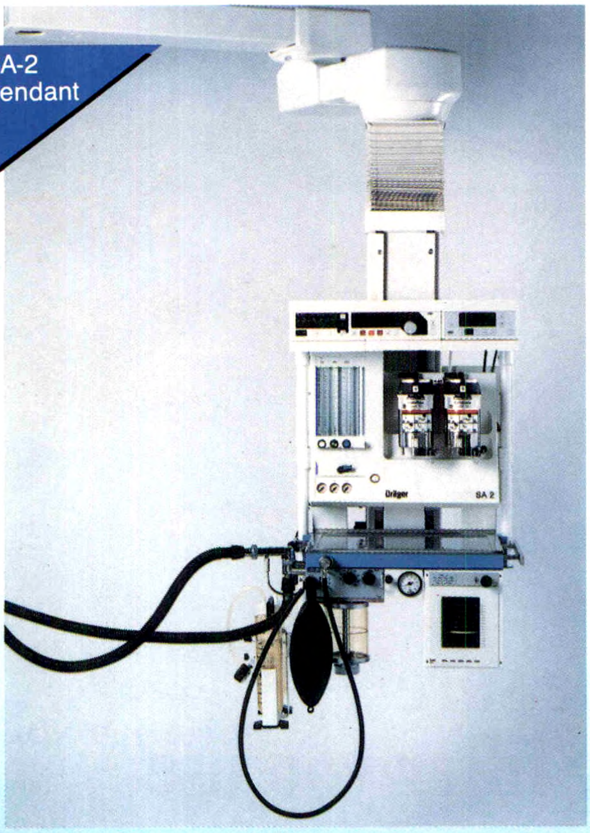
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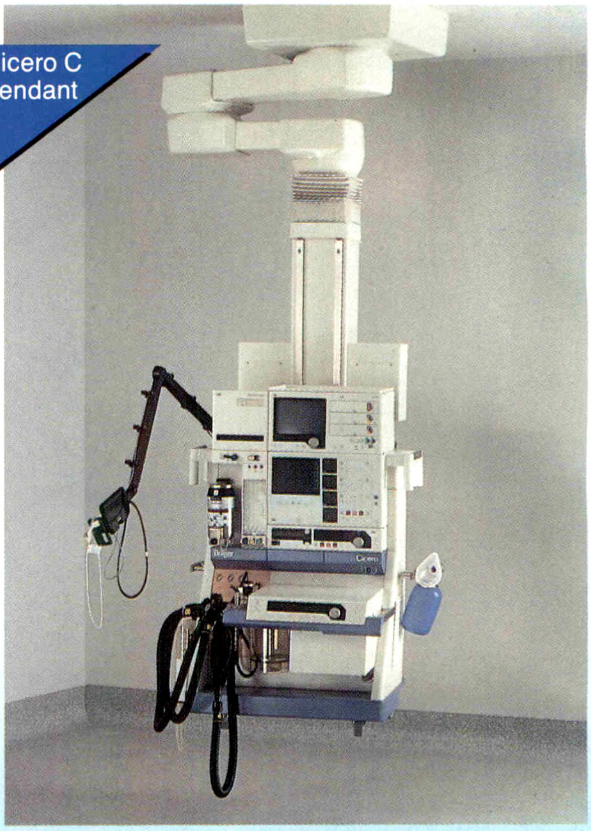
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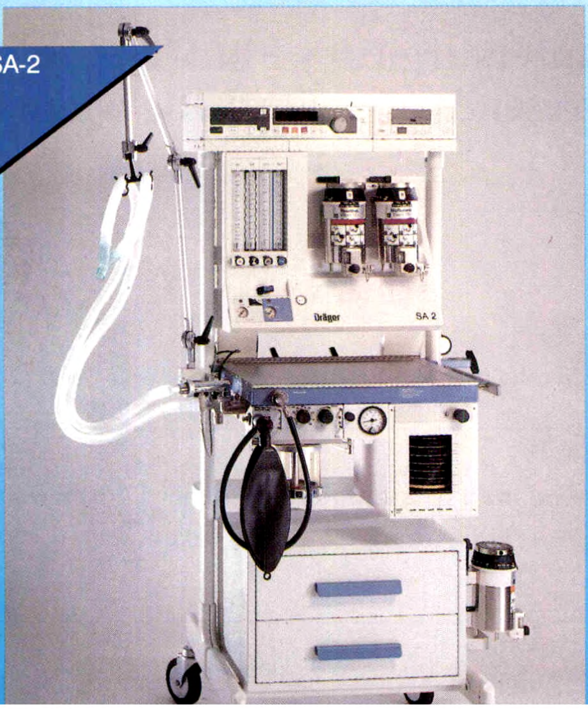
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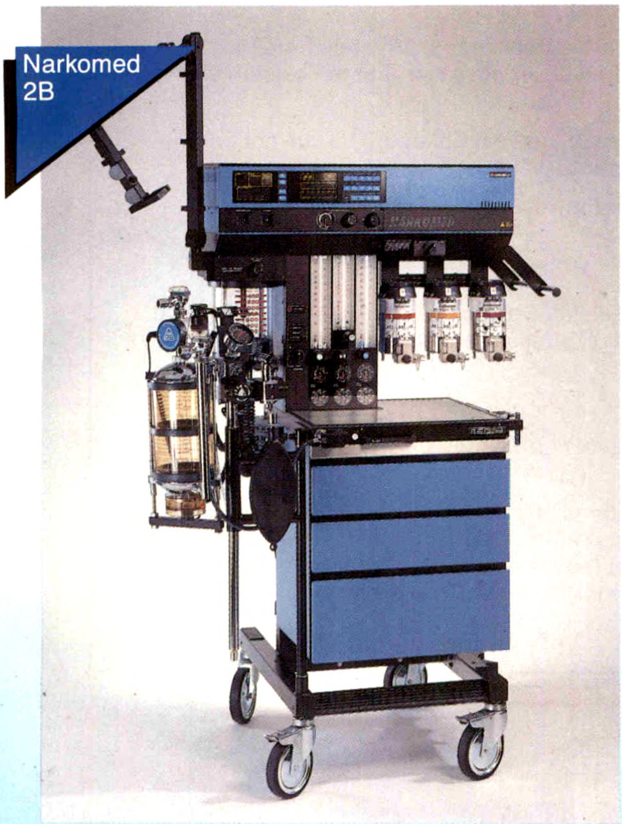

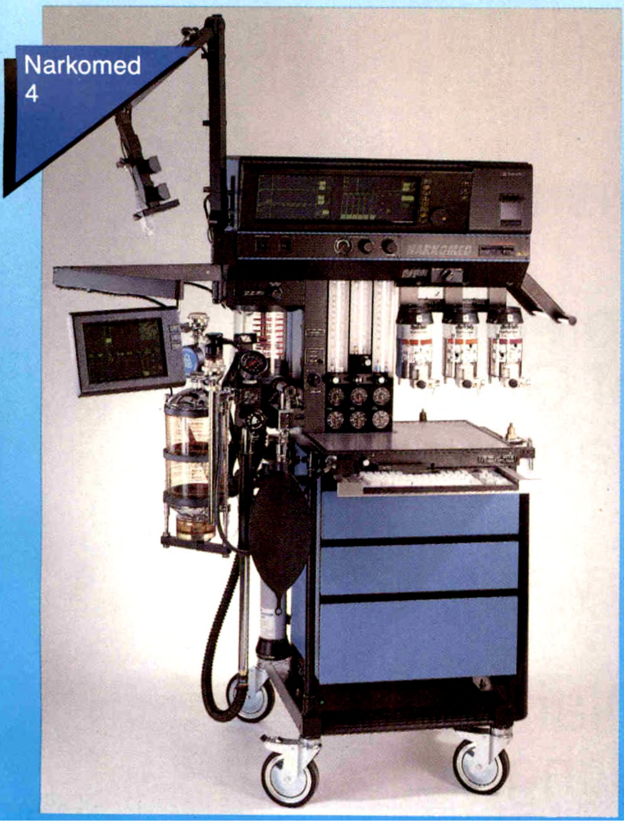

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Anaesthesia, 1992, Volume 47, pages 729–731

Editorial

Learning fibreoptic intubation: fundamental problems

Failed tracheal intubation still results in significant morbidity and mortality [1]. Several pre-operative tests have been proposed to identify patients at risk [2–5]. However, these have not gained general acceptance because of the incidence of false-positive results [6]. In a recent article, Frerk assessed two simple bedside tests for the prediction of difficult intubation and, in the cases studied, the two tests combined had a greater specificity than either test used alone [7]. If these tests taken together provide a more reliable method of predicting difficult intubation, how should such a patient be managed? A logical answer would be to perform an awake fibreoptic intubation.

The availability of the fibreoptic bronchoscope represents a significant landmark in the search for a solution to difficult intubation. Several excellent articles have discussed the problem of how to instruct trainees in the technique [8–10], but for some hospitals, problems may appear at an even more fundamental level. A standard intubating bronchoscope, light source, adaptor, suction, sterilising equipment and purpose-built trolley costs about £10,000. The first hurdle may therefore be the initial purchase. A diagnostic and therapeutic return on this order of investment may not be immediately obvious. Managers, and sometimes colleagues in other specialties, may have to be convinced in the competition for limited equipment budgets. The case is probably best presented in a written submission, giving a succinct account of the clinical and medicolegal problems of failed intubation.

Once acquired, the bronchoscope must be handled and maintained with care. It is a delicate instrument, consisting of insulated glass fibres bound into a flexible bundle. In addition there is a light guide cable, a working channel which is used for suction, local anaesthetic injection or oxygen insufflation, and angulation wires to allow movement of the tip in an anterior–posterior plane. Actual specifications such as length, diameter and tip angulation, can vary. Those designed for intubation tend to be longer (600 mm compared with 550 mm), of smaller diameter (4 mm compared with 5–6 mm), and possess lesser degrees of tip deflection and hence field of view (75′ compared with 90–120′), than diagnostic bronchoscopes.

Meticulous handling, cleaning and sterilisation are essential, otherwise repair costs will be high. It is not an instrument for the casual, unsupervised user and so a strict policy on its availability may need to be defined. The insertion cord will only tolerate gentle bending. Light fibres are easily damaged and each additional individual broken one causes an incremental deterioration in the optical image. Forcible bending of the distal tip may fracture the control wires. Following use, a scrupulous and invariable routine must be observed. The bronchoscope must always be tested for leaks before immersion in sterilising solution as seepage through breaches in the external casing will cause major damage to the optical system.

Before trainees can be taught to use the fibreoptic bronchoscope, senior members of staff must themselves first acquire the appropriate skills. Those who have learned by apprenticeship as a junior may underestimate the difficulty in acquiring a new skill, possibly unaided, as a consultant. Therefore, a priority is to provide opportunities for other senior staff to learn the technique. How should the technique be taught? Major differences appear to exist between the UK and the USA both in the teaching and practice of fibreoptic intubation. Local anaesthetic techniques seem to predominate in North America, whereas general anaesthesia features most commonly in the UK.

There are disadvantages to teaching fibreoptic bronchoscopy under general anaesthesia. Two main techniques are used. In one, deep anaesthesia is achieved in the spontaneously breathing patient and the bronchoscope is usually, but not always, inserted through the mouth. Skilled assistance is required to maintain the airway and pollution of the anaesthetic room often occurs due to leaks. Reported complications include loss of airway control, desaturation, laryngeal spasm, bronchospasm and arrhythmias [11]. In the second, the bronchoscope is inserted under light anaesthesia during apnoea produced by neuromuscular blockade, a technique which leaves only a limited time for bronchoscopic insertion and tracheal intubation.

After general anaesthesia has been induced, the soft palate, tongue and epiglottis approximate to the posterior pharyngeal wall [12]. Little air space is thus left in the oropharynx for manoeuvring the tip of the bronchoscope and the view tends to be obscured by the tissues. Several airways have been designed to overcome this problem and facilitate the insertion of the bronchoscope [13]. However, none of the approaches under general anaesthesia permit the unhurried, sequential identification of the nasal, pharyngeal and laryngeal structures, which is possible in the awake subject and essential when patients with abnormal anatomy or pathology are subsequently encountered. In addition, neither of the techniques prepare the trainee adequately to perform an awake fibreoptic intubation in a patient with a difficult airway.

Dykes and Ovassapian [14] recommend that a trainee learns initially on awake patients who have normal anatomy, but acknowledge the problem of finding suitable subjects on whom to gain experience. At their centre it became routine to perform an awake fibreoptic technique on all patients who required nasal intubation. If there are reservations about such an approach, the skills relevant to awake intubation may be acquired on patients undergoing diagnostic bronchoscopy. Such individuals readily accept that the ‘magic eye’ is used with local anaesthesia, and the judicious use of incremental doses of a diluted solution of midazolam usually ensures cooperation during the procedure and frequently amnesia as well.

Large numbers of diagnostic bronchoscopies are

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carried out each year, mostly under local anaesthesia and by physicians in respiratory medicine. In 1974 it was estimated that 15 000 patients a year in the UK might require diagnostic bronchoscopy [15]. However, a postal survey, which had a 90% response rate, indicated that at least 40 000 of these procedures had been undertaken during 1983 [16]. Increased cooperation between physicians and anaesthetists is advantageous to both doctors and patients alike. The benefit of the presence of a second doctor when a procedure is being carried out under sedation is well recognised. In the postal survey, the commonest major complication (described as life-threatening or a cause for concern) was respiratory depression from sedative–narcotic combinations. Routine administration of oxygen was confined to 18% cases, despite the fact that arterial desaturation frequently occurs during endoscopy under sedation. A consultant anaesthetist, supervising a trainee, could be responsible for the monitoring, sedation, administration of local anaesthesia, oxygenation and insertion of the bronchoscope through the vocal cords. Thereafter the physician would continue the procedure. The presence of the anaesthetist would permit the occasional very uncooperative patient to be given general anaesthesia, with the opportunity to offer reciprocal teaching of conventional tracheal intubation to members of the medical team.

To what extent can the trainee be prepared before his first fibreoptic bronchoscopy on an awake patient? Undoubtedly, the most difficult task is to learn to hold, manipulate and advance the bronchoscope. Since the angulation produced by the tip lever is in one plane only, lateral movement of the fibrescope can only be achieved by rotation, followed by appropriate flexion and extension. The arrow on the perimeter of the field of view is an invaluable guide to the orientation of the instrument. Excellent books and papers on the technique are available [5, 17] and are worthy of careful attention beforehand. Familiarity with the anatomy is essential and study of bronchoscopic photographs, both normal and abnormal, of the epiglottis, vocal cords and trachea is helpful. The basic technique of handling of the instrument can be learned using an airway training model and bronchial tree. These are relatively inexpensive and many hospitals already possess them for resuscitation training purposes. Trainees undergoing a graduated training programme in fibreoptic bronchoscopy using such models, were shown to have a greater initial success rate with awake fibreoptic intubation than those without such preliminary preparation [18]. In addition, other important aspects such as sedation, local anaesthetic application, and insertion of the tracheal tube after bronchoscopy has been achieved, can all be taught before a real patient is encountered.

There are other advantages to improving one's dexterity on patients undergoing diagnostic bronchoscopy. Diagnostic bronchoscopes are of larger diameter than those designed for intubation and a better image and wider field of view is obtained. The usual approach is via the nasal route, so the angulation required to enter the larynx is less than that needed using an oral technique and the tongue does not interfere with insertion.

Several useful tips can assist the beginner. When the nasal route is used, the position of the head and neck is important and differs from that required for conventional intubation. Full extension of the neck, either by removal of the pillow, or the use of a support under the shoulders, will open up the space around the glottis. The operator should insert a well-lubricated bronchoscope into the more patent nostril and negotiate the nasal passages under direct vision. Discomfort, trauma and bleeding are thus minimised. Navigation along the floor of the nose, below the inferior turbinate, often brings the epiglottis directly into sight. Loss of view may occur in the pharynx, as a result of the tip abutting onto mucosa or being covered with blood or secretions. Vision is often restored by slight withdrawal of the fibrescope from the mucosa. Blood or secretions can usually be removed by suction, although on occasions, saline may need to be injected through the working channel, or the instrument completely withdrawn for cleaning.

It is helpful to remember that, in adults, the distance between the nares and the epiglottis is about 15 cm. If structures are difficult to identify in the pharynx, the operator should be encouraged to pass the scope to about 12 cm, at which point recognisable structures often reappear. If the 15 cm mark has been passed and the glottis is still not visible, the bronchoscope is likely to be in the oesophagus. When the glottic structures have been identified, but difficulty is encountered passing the bronchoscope through the vocal cords, the patient should be asked to take a deep breath to bring about maximum abduction of the glottis. One of the commonest causes of failure of fibreoptic intubation is movement of the laryngeal structures as a result of inadequate topical anaesthesia [19]. In such cases further local anaesthetic should be introduced onto the vocal cords, via the working channel.

Once the technique has been mastered in patients with normal anatomy, anaesthetists will be anxious to apply it to those in whom there are clinical indications. Fibreoptic intubation is not, however, the answer to every airway problem. The technique should not be applied uncritically, particularly if the operator is relatively inexperienced. A discussion on the indications and possible contraindications for bronchoscopy is therefore an essential part of training. The most appropriate candidate for awake fibreoptic intubation is the patient in whom the potential intubation difficulties are anatomical in origin, such that direct vision of the vocal cords is impossible using the conventional laryngoscope. Structural or pathological abnormalities involving the neck, mandible, maxilla, or teeth may contribute to these difficulties. Those patients in whom there is a risk of damage to teeth or dental work may also be suitable candidates, since dental claims form a significant proportion of anaesthetic medicolegal practice.

Some suggested indications for fibreoptic intubation are more controversial. A case has recently been advanced for the awake intubation of all emergency patients who are at high risk from aspiration of gastric contents [20]. However, aspiration may still occur in the awake patient, and even the precaution of applying local anaesthetic only after the vocal cords have been visualised may not always protect a patient from massive regurgitation and aspiration. The use of the fibreoptic bronchoscope in patients with severe upper airway obstruction is also uncertain. Where there is critical upper airway narrowing as a result of oedema or tumours, instrumentation may precipitate complete obstruction even in the awake patient. Tumours may bleed or pieces might be directly dislodged by the bronchoscope. In the awake patient, interference with the upper airway in the presence of epiglottitis has traditionally been regarded as potentially dangerous. There are, however, advocates of awake intubation even in this condition [17]. It should be emphasised that such techniques are only for the experienced bronchoscopist and the presence of an ENT surgeon prepared to perform emergency tracheostomy is mandatory.

The aim of every anaesthetic department should be to provide a structured training programme in fibreoptic bronchoscopic intubation. Opportunities to cooperate with the chest physicians who provide diagnostic bronchoscopy services should be explored. The acquisition of confidence and skill in the technique will encourage an expansion of clinical indications. The threshold for the use of fibreoptic intubations should be lowered such that the technique is regularly practised and every anaesthetist becomes skilled in the art. Bedside tests for predicting intubation difficulty will only be of value if positive information elicits a logical response—if in doubt, intubate awake.

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Regurgitation and oesophageal rupture with cricoid pressure: a cadaver study

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Summary

The efficacy of cricoid pressure was studied in 10 adult cadavers. The oesophageal pressure that would result in regurgitation during measured values of cricoid pressure was determined. Oesophageal pressure, recorded by a 2 mm diameter oesophageal tube, was increased by oesophageal distension with saline, and incremental levels of cricoid force, 20, 30 and 40 Newtons, were applied with a cricoid yoke. With each 10 Newton increment of cricoid force there was a significant rise in the oesophageal pressure required to provoke regurgitation ($p < 0.01$). Thirty Newtons of cricoid force prevented regurgitation of saline in all cadavers with oesophageal pressures of up to 40 mmHg. Rupture of the oesophagus occurred in three cadavers: one at 30 and two at 40 Newtons of cricoid force, but there was no rupture at 20 Newtons of cricoid force. In the other seven cadavers oesophageal pressures were also studied with a 4.6 mm diameter (14 FG) oesophageal tube, which did not reduce the efficacy of cricoid pressure in preventing regurgitation.

Key words

Larynx; cricoid pressure.
Complications; oesophageal rupture, regurgitation.

Anaesthesia with neuromuscular blocking drugs relaxes the upper oesophageal sphincter [1] and can allow the regurgitation of oesophageal contents into the pharynx. Cricoid pressure compensates for this fall in sphincter tone and is designed to prevent regurgitation before the insertion of a tracheal tube. The cricoid force required has been determined in two studies of anaesthetised patients by measuring sphincter pressure while applying incremental levels of cricoid force with a cricoid yoke [1, 2]. In both of these studies, by necessity, the experimental conditions did not relate to the usual clinical situation; sphincter pressure was measured by water perfused catheters which only give an estimate of oesophageal pressure during regurgitation, also the airway was protected by a tracheal tube while in clinical practice cricoid pressure is applied before intubation.

In one patient undergoing oesophagectomy with the cardia clamped, Sellick distended the oesophagus with saline through an oesophageal tube to a pressure of 100 cmH_2O (74 mmHg), and found that firm cricoid pressure controlled regurgitation [3]. Studies of both infant and adult cadavers have since confirmed that firmly applied cricoid pressure can prevent regurgitation during distension of the oesophagus with saline, with or without an oesophageal tube [4–6]. None of these studies has related the applied cricoid force to oesophageal pressure at regurgitation.

The present investigation was undertaken to determine what level of oesophageal pressure would result in regurgitation of saline at three levels of cricoid force applied with a cricoid yoke.

Method

Permission was given by the hospital ethics committee to study cadavers about to undergo hospital postmortem examinations. Permission was also given by the pathologist responsible for each examination. Cadavers were studied within 3 days of death and within 1 h of removal from the refrigerator.

Measurement of cricoid pressure

A hand-held cricoid yoke [1] was used to apply cricoid pressure. The force was applied to the cricoid cartilage through a 1 cm wide concave ridge of firm rubber, which was covered by a shaped foam pad. The applied force was measured by a load cell in the handle. The load cell was connected by a wire to a separate box which housed the amplifier and battery and displayed the applied force in

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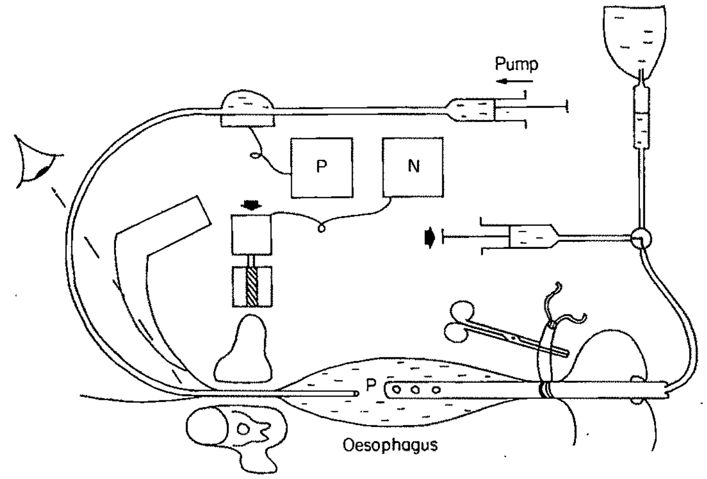

Fig. 1. Oesophageal cannulation with the tube used for oesophageal distension inserted from below and the tube to measure oesophageal pressure (P) inserted from above. The cricoid yoke is shown applying force (N) to the cricoid cartilage.

Newtons (N) on a gauge. The cricoid yoke was zeroed and then calibrated on weighing scales before each use (1 kg = 9.81 N).

Oesophageal cannulation

The cadaver was positioned supine with a 5 cm diameter sand bag under the neck but with no pillow under the head. A midline abdominal incision was made from the sternum to below the umbilicus. The cardia of the stomach was mobilised by blunt dissection and a 5 mm wide cotton tape was placed loosely around it with two turns. A hole was made in the fundus of the stomach through which a 15 mm diameter reinforced tube was inserted and passed into the mid-oesophagus. The tape was then secured tightly around it (Fig. 1). The outer end of the tube was connected to a 3 way tap, with a 50 ml syringe on the second port and a giving set with one litre of saline on the third. The oesophagus was then rinsed with saline and the regurgitated fluid removed from the pharynx with a sucker.

Oesophageal pressure was measured through one of two sizes of oesophageal tube inserted into the upper oesophagus through the mouth using a laryngoscope and Magill's forceps and positioned with the tip 25 cm from the mouth (Fig. 1). Tube A was of 2 mm diameter (Lectrocath, Vigon) with the male Luer connector cut off; tube B was a 14 FG Salem sump tube (4.6 mm diameter) with the pressure measured through the 1 mm diameter air vent, the main lumen of the tube being filled with water and spigotted. The tubes were connected to a calibrated transducer and perfused at $0.6\,\text{ml.min}^{-1}$ by a syringe pump (Fig. 1). The transducer was zeroed for each tube before insertion with the end positioned at the midpoint of the side of the neck.

Pilot case

In a pilot case (not included in the results as the method was later changed) only one oesophageal tube could be studied due to a sudden loss of oesophageal pressure with rupture of the oesophagus. As a consequence we decided that tube A would be studied first in all cases to standardise the conditions of the study to investigate the oesophageal pressures needed to cause either regurgitation or oesophageal rupture during cricoid pressure. This small tube was chosen so as not to interfere with the efficacy of cricoid pressure. Tube B would only be studied if the oesophagus was still intact after studying tube A. This was of interest because a similar size tube is used clinically as a nasogastric tube. As their order of study would not be randomised, there could be no formal comparison between the two oesophageal tubes.

Procedure

The pharynx was observed continuously with a laryngoscope and regurgitation of saline could easily be detected without using dye. The oesophagus was gradually distended with saline using the 50 ml syringe. The oesophageal pressure was continuously monitored with both a screen and a digital display. When regurgitation first occurred the oesophageal pressure at that moment was recorded. The pharynx was then emptied with the sucker before the sequence was repeated at each level of cricoid force (0, 20, 30 and 40 N) applied with the cricoid yoke. If the oesophagus was still intact after these measurements, tube A was removed and replaced by tube B and the whole procedure repeated. Cricoid pressure alone did not raise the pressure in either tube indicating that cricoid pressure did not compress the measuring lumen of the oesophageal tubes.

Statistics

The paired *t*-test was used to compare oesophageal pressures at regurgitation between the different levels of cricoid force. Significance was assumed at the level of $p < 0.05$.

Results

The investigation was attempted in 12 cadavers but results could not be obtained in two: one male with chronic bronchitis could not be studied as the cricoid cartilage was too close to the sternum preventing the correct application of the cricoid yoke; in the other, also male, the tube could not be passed from the mouth into the oesophagus and a

Table 1. Cadaver details, mean (range).

n	10
Number female	7
Age; years	80 (60–87)
Weight; kg	52 (40–61)
Hours after death	45 (18–64)
Refrigerator temp; °C	4.0 (2–8)

Table 2. Oesophageal pressure at regurgitation in mmHg, with tube A or B, at each increment of cricoid force in seven cadavers, mean (SD) and (range).

Cricoid force	Tube A	Tube B
0 N	2 (2) (0–7)	1 (1) (0–2)
20 N	39 (11) (26–60)	49 (17) (34–75)
30 N	56 (15) (42–85)	72 (16) (44–95)
40 N	74 (23) (53–120)	96 (23) (80–135)

false passage was made. The details of the other 10 cadavers are shown in Table 1.

The oesophageal pressures at regurgitation with tube A are shown in Figure 2. In the absence of cricoid pressure, regurgitation occurred at low levels of oesophageal pressure; with increasing levels of cricoid force there was a progressive rise in the oesophageal pressure required to provoke regurgitation in all subjects. Rupture of the oesophagus or stomach occurred in three of the 10 cadavers, all three were female. Rupture was identified by a sudden loss of oesophageal pressure and the appearance of saline in the peritoneal cavity. At 20 N of cricoid force there was no case of oesophageal rupture, regurgitation occurred in all 10 cadavers. Rupture of the oesophagus occurred in one cadaver, studied 64 h after death, at an oesophageal pressure of 105 mmHg with 30 N of cricoid force and in another cadaver, studied 60 h after death, also with an oesophageal pressure of 105 mmHg at 40 N of cricoid force (Fig. 2). In the third cadaver, studied 30 h after death, rupture occurred at a pressure of 86 mmHg with a cricoid force of 40 N; in this cadaver the tape was secured below the cardia because of a shortened oesophagus with a large hiatus hernia, and the stomach above the tape ruptured. Leakage past the tape securing the 15 mm tube did not occur in any cadavers. Once the oesophagus or stomach had ruptured the cadaver could no longer be studied.

Seven cadavers were studied with both oesophageal tubes A and B; the oesophageal pressures at regurgitation are shown in Table 2. In each cadaver there was an increase in oesophageal pressure at regurgitation with each increment of cricoid force with either tube A or tube B; these increases were significant ($p < 0.01$). The oesophageal pressures at regurgitation were higher with the larger oesophageal tube.

Discussion

The maximum gastric pressure recorded while supine in starved patients is 25 mmHg [7, 8] and gastric distension by 750 ml can increase that by 10 mmHg [9] so that with a full stomach, gastric pressure while supine at rest may reach 35 mmHg. During spontaneous gastro-oesophageal reflux, oesophageal pressure can equal gastric pressure with the development of a common cavity [10]. In the present study, 30 N of cricoid force prevented regurgitation in all cadavers with oesophageal pressures of up to 40 mmHg. Therefore 30 N of cricoid force should prevent the passive regurgitation of oesophageal contents into the pharynx after the upper oesophageal sphincter relaxes with the induction of anaesthesia and neuromuscular blockade. Values of 40 and 44 N of cricoid force have previously been recommended [1, 2], but if 30 N is effective then it is to be preferred since 44 N applied with a cricoid yoke can cause compression of the larynx and difficulties with intubation in 10% of patients [11].

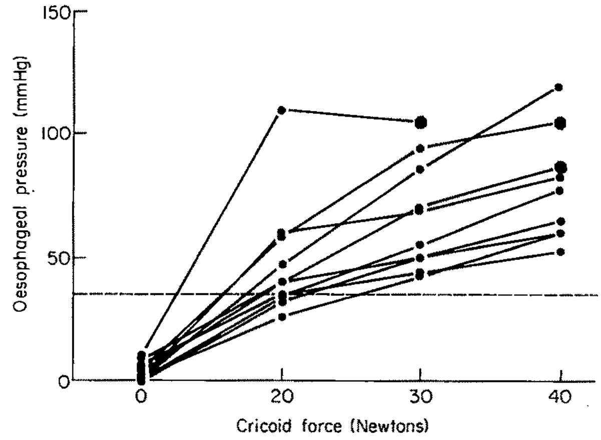

Fig. 2. A graph of oesophageal pressure at each increment of cricoid force in each of the 10 cadavers with tube A. The small round symbols represent oesophageal pressure at regurgitation and the large round symbols represent oesophageal pressure at rupture of the oesophagus or stomach. The horizontal dashed line is at 35 mmHg and represents the maximum gastric pressure while supine at rest for comparison.

The clinical relevance of this study depends on whether the compression of the upper oesophageal sphincter by the cricoid cartilage against the vertebral column is similar in the cadaver at 4°C to the anaesthetised and paralysed patient. In a study of 24 such patients positioned without a pillow [1] the median values of the upper oesophageal sphincter pressures were 40 mmHg at 20 N, 56 mmHg at 30 N and 77 mmHg at 40 N of cricoid force applied with the same cricoid yoke; there was a wide variation of sphincter pressure values which were not normally distributed. In the present study the mean oesophageal pressures at regurgitation with tube A were almost identical (Table 2). The wider variation of sphincter pressure values may be due to problems in recording occlusion pressures with a manometry catheter rather than to a functional difference between patients and cadavers.

Our results can be compared to the two other studies of adult cadavers where oesophageal pressure was indirectly recorded during oesophageal distension with saline and the firm application of cricoid pressure. Salem *et al.* [6] showed that out of six adult cadavers, none regurgitated at an oesophageal pressure of 74 mmHg with an 18 FG oesophageal tube in place; our results showed the same with the 14 FG oesophageal tube when 40 N of cricoid force was applied (tube B, Table 2). Fanning [4] studied one infant and four adult cadavers with no oesophageal tube and showed that regurgitation occurred at oesophageal pressures between 37 and 70 mmHg (mean 55 mmHg); these results are similar to ours with 30 N of cricoid force and the small oesophageal tube (tube A, Table 2).

As we did not randomise the order of the two oesophageal tubes we cannot claim that a 14 FG oesophageal tube increases the efficacy of cricoid pressure in preventing regurgitation. However, it does not seem to decrease the efficacy of cricoid pressure. Sellick [12] originally suggested that oesophageal tubes can increase the risk of regurgitation by 'tripping' both the upper and lower oesophageal sphincters and also interfering with oesophageal compression during the application of cricoid pressure. Since then there has been little evidence to support this: Satiani *et al.* [13] in a randomised study of nasogastric tube drainage during surgery in 146 patients demonstrated no significant difference in the incidence of regurgitation of dye with or without the nasogastric tube; Salem *et al.* have shown in both infant [5] and adult [6] cadavers with oesophageal tubes that cricoid pressure can still prevent regurgitation. Nasogastric tubes are not occluded by cricoid pressure [6] and if left open to atmospheric pressure can vent liquid or gas and can therefore limit increases in gastric pressure during induction of anaesthesia.

Cricoid pressure will offset the reflex relaxation of the upper oesophageal sphincter that occurs during vomiting. The resulting rise in oesophageal pressure may cause rupture of the oesophagus, as has been reported in an 81-year-old female with a bleeding gastric ulcer who died [14]. In this case the stomach was initially aspirated with the nasogastric tube which was then removed; cricoid pressure was applied 'firmly' before induction, the patient retched three times after the injection of the intravenous anaesthetic and cricoid pressure was continued until the patient had been turned to the lateral position and vomit did not appear until cricoid pressure was released (personnel communication from Dr Wareham). In the present study we have demonstrated rupture of the oesophagus or stomach in three cadavers during 30 and 40 N of cricoid force. With 20 N of cricoid force regurgitation of saline limited the oesophageal pressure and therefore prevented rupture in all 10 cadavers. As the tissues of the cadaver are more friable than those of a living patient, regurgitation of vomit is likely to occur before oesophageal rupture when 20 N of cricoid force is applied to the conscious patient who retches. Clinically, rupture of the oesophagus in association with cricoid pressure is extremely rare, probably because cricoid forces of over 20 N are poorly tolerated by conscious subjects [15].

These findings suggest that no more than 20 N of cricoid force should be applied to the awake patient, increasing to 30 N after loss of consciousness to prevent the passive regurgitation of oesophageal contents as the upper oesophageal sphincter relaxes. If a nasogastric tube is present before induction, the stomach should be emptied as far as possible and the nasogastric tube withdrawn to the mid-oesophagus (30 cm from the nares in adults) and the oesophagus also emptied. If the tube is left open to atmospheric pressure and in this position, it will not decrease the efficacy of cricoid pressure and should limit any rise in oesophageal pressure during the induction of anaesthesia.

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Thoracic electrical bioimpedance measurement of cardiac output and cardiovascular responses to the induction of anaesthesia and to laryngoscopy and intubation

D. J. SANDERS, C. F. JEWKES, J. W. SEAR, F. VERHOEFF AND P. FOËX

Summary

Noninvasive methods of determining cardiac output (by thoracic electrical bioimpedance) and arterial pressure (by intermittent oscillometry) were used to record minute-by-minute changes in heart rate, mean arterial pressure, stroke volume, cardiac output and systemic vascular resistance following induction of general anaesthesia and laryngoscopy and intubation in 60 healthy female patients who were either unpremedicated, or premedicated with temazepam or papaveretum–hyoscine. Anaesthesia was induced with a sleep dose (3–5 mg.kg^{-1}) of thiopentone and maintained with 70% nitrous oxide in oxygen with 0.5–1% enflurane. Tracheal intubation was facilitated by administration of vecuronium 0.1 mg.kg^{-1}. Mean arterial pressure and cardiac output decreased maximally 5 min after induction in all premedication groups by mean estimates of 21–25% and 14–22% respectively. Heart rate increased initially one minute after induction, but decreased to less than the baseline value 5 min after induction. Systemic vascular resistance was unchanged. The stimulus of laryngoscopy and tracheal intubation was accompanied by a significant pressor response and tachycardia one minute after intubation (with mean increases in mean arterial pressure and heart rate of 29–34% and 22–33% respectively). The increase in mean arterial pressure was secondary to an increase in systemic vascular resistance (36–57%), and was accompanied by a decrease in stroke volume (−25 to −31%). These changes were significant in all three groups. Cardiac output decreased only in unpremedicated patients. There were wide variations in the different haemodynamic indices. The 5th and 95th centiles for the decreases in mean arterial pressure and cardiac output during induction were −17 to −26, −21 to −33, and −21 to −35 mmHg, and −0.7 to −2.0, −0.7 to −2.3, and −0.2 to −1.3 l.min^{-1} respectively in unpremedicated patients and those premedicated with papaveretum–hyoscine, or temazepam. Corresponding values for increases in mean arterial pressure and systemic vascular resistance, and decreases in stroke volume following laryngoscopy and intubation, were 16 to 33, 16 to 31.5, and 15 to 31 mmHg; 5.0 to 8.6, 3.5 to 10.2, and 4.3 to 7.8 mmHg.min.l^{-1}; and −19 to −31, −11 to −32.5, and −9 to −21 ml respectively.

Key words

Measurement techniques; thoracic electrical bioimpedance.
Intubation; tracheal, complications.

The profound cardiovascular changes which can occur at induction of anaesthesia and after laryngoscopy and tracheal intubation have been studied extensively in terms of fluctuations in arterial pressure and heart rate [1–3]. However, such measurements may conceal significant variations in cardiac output ($\dot{Q}$) and systemic vascular resistance (SVR). Further elucidation of the cardiovascular responses to induction agents and to laryngoscopy and intubation requires the simultaneous and repeated measurement of cardiac output, arterial pressure and heart rate. Few studies have attempted this, as most techniques available for measuring cardiac output are unsuitable either because they do not permit frequent repeated determinations (Fick method and dye dilution) or are too invasive for routine use (thermodilution and electromagnetic flowmeters).

Consequently, we have explored the use of thoracic electrical bioimpedance (TEB) cardiography combined with an oscillometric method to measure changes in cardiac output and arterial pressure during induction of anaesthesia, laryngoscopy and tracheal intubation. To our knowledge, no other study has reported the minute-by-

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minute assessment of the haemodynamic responses in large numbers of healthy subjects. A preliminary account of some of this work has already been presented [4].

Patients and methods

The study was approved by the local ethics committee and informed verbal consent was obtained from all patients.

The study population consisted of female patients aged 20–70 years (ASA class 1 or 2) who required tracheal intubation as part of anaesthesia for elective gynaecological surgery. Patients with hypertension, peripheral vascular or cardiac disease and those taking drugs with cardiovascular effects were excluded, as were patients with a difficult airway or those who required rapid sequence induction. As the intention was to explore the haemodynamic changes in a representative population of anaesthetised patients, premedication was prescribed on clinical grounds and consisted of either no premedication (group U; unpremedicated), oral temazepam 10–20 mg (group T) or intramuscular papaveretum 10–15 mg with hyoscine 0.2–0.3 mg (group P).

A Dinamap (model 845XT, Critikon), which employs an intermittent oscillometric technique, was used to measure systolic, diastolic and mean arterial pressures. Heart rate, stroke volume (SV), cardiac output and thoracic fluid index (TFI) (representing the basal thoracic impedance) were determined by the TEB method using a BoMed NCCOM3 (BoMed .Medical Manufacturing Ltd, Irvine, CA, USA). To reduce the effects of ventilation on cardiac output measurements, the NCCOM3 was programmed to average over 16 cardiac cycles and the resulting values were listed on a Thinkjet printer (Hewlett Packard). The mean value of three successive determinations, made during the cuff deflation cycle of the Dinamap, was employed in subsequent analyses. The reproducibility between values taken successively in the absence of an intervention has been shown previously to be 3.4%, 4.8%, 4.7% and 5.1% for mean arterial pressure, heart rate, stroke volume and cardiac output respectively [5].

The electrocardiogram (ECG) and rate of change of impedance (dZ/dt) signals available from the NCCOM3 were monitored with a dual channel strip chart recorder to ensure freedom from artifacts and consistent signal quality during the induction sequence.

A standardised sequence of measurement and drug administration was used for all patients. Following cannulation of a vein and placement of the TEB electrodes and blood pressure cuff, two sets of baseline measurements were made, separated by a few minutes, while the patient rested in a supine position. The means of these two determinations were used in subsequent analyses as 'resting values'. Fentanyl 100 μg was given and a further measurement made one minute later. Anaesthesia was induced with a dose of thiopentone sufficient to obtund the eyelash reflex (3–5 $mg.kg^{-1}$) and further measurements were made after one and 3 min while the patient breathed 70% nitrous oxide in oxygen supplemented with enflurane 0.5–1.0%. Vecuronium 0.1 $mg.kg^{-1}$ was given 3 min after induction, and ventilation was assisted. Further measurements were made 5 min after induction, immediately before laryngoscopy and tracheal intubation, and then at one, 3 and 5 min after orotracheal intubation.

Systemic vascular resistance has been calculated as mean arterial pressure divided by the corresponding cardiac output, and expressed as $mmHg.min.l^{-1}$. Statistical comparisons within premedication groups were performed using ANOVA, and where indicated using the paired *t*-test, with the Bonferroni correction for multiple comparisons. Differences between groups have been compared using the Mann–Whitney *U*-test.

Table 1. Demographic characteristics of the three treatment groups. Data are presented as mean (SD).

	Premedication treatments		
	Unpremedicated (U)	Papaveretum (P)	Temazepam (T)
(*n*)	20	20	20
Age; years	34.9 (10.4)*	41.7 (10.8)	45.5 (10.8)
Weight; kg	64.6 (9.9)	64.8 (8.4)	64.3 (9.2)
TFI; Ω	31.9 (4.0)	32.7 (5.0)	30.4 (4.1)

*$p < 0.01$ compared with group T.
TFI, thoracic fluid index.

Results

Sixty-five patients were studied. Five patients were excluded from analysis, one because the induction protocol was violated, two because of irregularity of the dZ/dt waveform after induction and two because of abnormal TFI values, which were substantially less than the accepted lower limit for healthy subjects. The remaining 60 patients were distributed evenly between the three premedication groups.

Demographic characteristics are shown in Table 1, and resting haemodynamic parameters in Table 2. The unpremedicated patients were slightly younger ($p < 0.01$) but had similar mean weights and TFI values. Resting heart rate (HR) and mean arterial pressure (MAP) were similar in all premedication groups. Stroke volume, cardiac output and systemic vascular resistance were also comparable in groups T and P, but the unpremedicated patients had a significantly greater resting cardiac output and a lower SVR ($p < 0.05$).

All groups of patients exhibited similar haemodynamic changes during the induction–intubation sequence irrespective of premedication. Following induction of anaesthesia with the combination of thiopentone and fentanyl, there were decreases in MAP and $\dot{Q}$, which were maximal 5 min after induction. SVR was unchanged. HR increased in all groups one minute after induction of anaesthesia, but was lower than pre-induction values before laryngoscopy and intubation. SV decreased in all groups one minute after induction, but by 5 min after induction it was not significantly different from baseline except in group P ($p < 0.02$).

Laryngoscopy and tracheal intubation resulted in increases in HR, MAP and SVR, and an accompanying decrease in SV. As a result of the changes in HR and SV, $\dot{Q}$ decreased only in group U. The increase in HR but not the rise in MAP exceeded baseline values in groups P and T. The magnitudes of the increases in MAP and HR were similar in all groups.

Five minutes after laryngoscopy and intubation, SVR had returned to pre-intubation values, which did not differ from baseline values, while MAP, HR and $\dot{Q}$ were significantly lower than resting values. Table 2 lists heart rate,

Table 2. Values of haemodynamic parameters during induction and the laryngoscopy–intubation sequence. Data are presented as mean (SD).

Parameter	Group	A	B	C	D
MAP; mmHg	U	96 (12)	76 (11)*	102 (19)†	76 (12)*
	P	94 (11)	70 (14)*	94 (18)†	72 (10)*
	T	98 (11)	75 (12)*	97 (15)†	76 (10)*
HR; beat.min^{-1}	U	86 (12)	73 (11)*	94 (17)†	72 (13)*
	P	77 (16)	69 (14)*	92 (18)*†	66 (14)*
	T	82 (13)	76 (9)*	93 (12)*†	75 (10)*
SV; ml	U	91 (26)	86 (25)	59 (20)*†	82 (26)
	P	81 (24)	71 (20)**	50 (15)*†	70 (18)
	T	70 (15)	65 (14)	49 (7)*†	64 (12)
$\dot{Q}$; l.min^{-1}	U	7.7 (1.9)	6.2 (1.5)*	5.3 (1.4)*†	5.8 (1.5)*
	P	6.0 (1.5)	4.7 (1.0)*	4.4 (0.8)*	4.5 (1.0)*
	T	5.8 (1.4)	5.0 (1.3)*	4.6 (1.0)*	4.8 (1.2)*
SVR; mmHg.min.l^{-1}	U	13.3 (3.7)	12.9 (3.7)	20.2 (6.3)*†	13.7 (3.5)
	P	16.7 (5.1)	15.6 (4.9)	22.5 (6.9)*†	16.5 (4.5)
	T	18.0 (5.5)	16.0 (4.8)	21.8 (5.0)*†	16.6 (4.4)

A, resting state; B, 5 min after induction; C, 1 min after intubation; D, 5 min after intubation.

MAP, mean arterial pressure; HR, heart rate; SV, stroke volume; $\dot{Q}$, cardiac output; SVR, systemic vascular resistance.

*$p < 0.01$; **$p < 0.05$ compared to resting state value (A).

†$p < 0.01$; difference between pre-intubation and postintubation values.

mean arterial pressure, stroke volume, cardiac output and systemic vascular resistance at four key points during the induction–intubation sequence.

The relationships between the individual haemodynamic parameters and the sequence of induction and intubation are illustrated in Figure 1 for the 20 patients in group U.

One aim of the study was to examine the variability in haemodynamic responses to laryngoscopy and intubation in a large group of subjects. The absolute differences for the five haemodynamic variables following induction, laryngoscopy and intubation are shown as the median and 5th and 95th centiles (Table 3). The median differences vary among the groups, but the changes follow consistent trends. The 5th and 95th centile ranges of all the differences are wide but of similar magnitude in the three premedication groups.

Discussion

Our results show that in healthy patients, in whom anaesthesia has been induced with thiopentone, the hypertensive response to laryngoscopy and intubation arises solely from an abrupt increase in systemic vascular resistance.

The noninvasive techniques used to measure cardiac output and arterial pressure are fundamental to both the technique and ethical feasibility of this study and therefore deserve some comment. Practical TEB methods of measuring cardiac output were originally developed in the 1960s by Kubicek [6], although they were not used widely. Recently, theoretical modifications and technical advances have produced the compact computerised device (BoMed NCCOM3) used in this study [7].

We have shown previously that the BoMed TEB correlates well with thermodilution methods for cardiac output, and has a reproducibility in resting healthy individuals of < 5%, and a reproducibility of 8.7% when used under comparable conditions at different sampling times [5]. Other studies have confirmed the reliability of TEB in following changes in cardiac output during both exercise and anaesthesia [8–11].

Arterial pressure was also measured noninvasively using the Dinamap 845 which has been shown to yield values that correlate well with intra-arterial pressure measurements [12]. Since the 95% confidence interval for individual

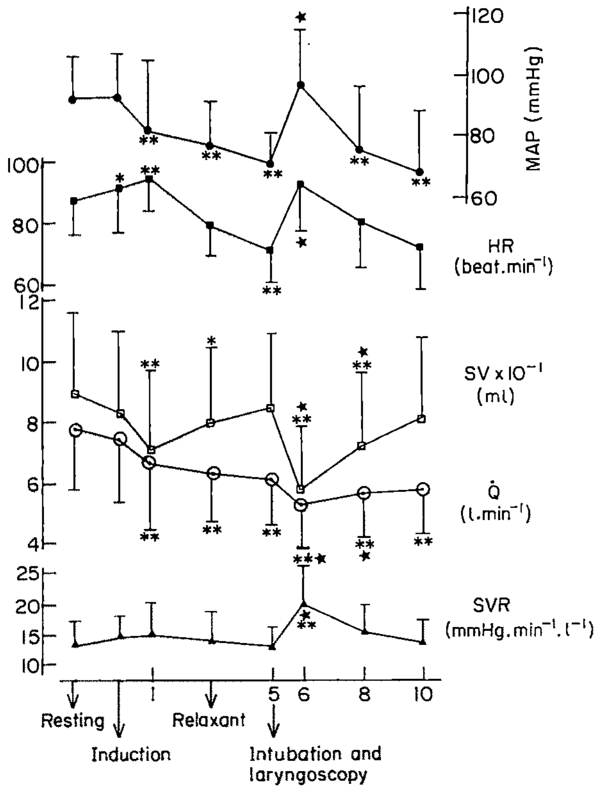

Fig. 1. Values of haemodynamic parameters for the 20 patients in Group U during the induction and intubation sequence. ● = mean arterial pressure (MAP); ■ = heart rate (HR); □ = stroke volume (SV); ○ = cardiac output ($\dot{Q}$); ▲ = systemic vascular resistance (SVR). Bars represents SD. Time zero on the horizontal axis corresponds to the start of induction, and +5 to the start of laryngoscopy and intubation. *$p < 0.01$ and **$p < 0.005$ compared with resting value; ✱ $p < 0.005$ compared with pre-intubation value.

Table 3. Median values (5th and 95th centile range) of the absolute differences between haemodynamic parameters before induction and 5 min after induction, and before intubation and one minute after intubation.

		Induction			Intubation		
	Premedication	Median	5th	95th	Median	5th	95th
MAP; mmHg	U	−20	−17	−26	+24	+16	+33
	P	−27	−21	−33	+20	+16	+31.5
	T	−26.5	−21	−35	+24	+15	+31
HR; beat.min^{-1}	U	−20	−11	−24	+20	+13	+30
	P	−7	−4.5	−11	+30	+16	+34.5
	T	−6	−1	−17	+19.5	+9	+27
SV; ml	U	0	+6	−9	−23	−19	−31
	P	−7	−3.5	−27	−17	−11	−32.5
	T	−2	+2	−16	−15.5	−9	−21
$\dot{Q}$; l.min^{-1}	U	−1.3	−0.7	−2.0	−0.8	−0.4	−1.2
	P	−1.7	−0.7	−2.3	−0.3	0	−0.8
	T	−0.7	−0.2	−1.3	−0.3	+0.1	−0.8
SVR; mmHg.min.l^{-1}	U	−0.9	+1.0	−3.0	+7.2	+5.0	+8.6
	P	−0.7	+0.8	−4.5	+7.2	+3.5	+10.2
	T	−2.9	+0.6	−5.5	+5.6	+4.3	+7.8

MAP, mean arterial pressure; HR, heart rate; SV, stroke volume; $\dot{Q}$, cardiac output; SVR, systemic vascular resistance.

Dinamap measurements is 16 mmHg and pressures may change during determination, some additional variability is introduced relative to the use of direct pressure measurement. However, it was felt that these limitations were compensated for by our ability to study repeated observations in a large number of patients.

Most studies which have measured changes in cardiac output during induction of anaesthesia have done so under steady state conditions at rest and then when parameters have stabilised or reached an assumed minimum after induction [2, 13]. The ability of noninvasive techniques to follow changes in cardiac output on a minute-by-minute basis have allowed us to describe haemodynamic responses to induction and intubation more closely than has been possible previously. By performing a series of determinations at rest and one, 3 and 5 min after induction, we have been able to produce a profile of the haemodynamic changes. The changes observed during induction of anaesthesia are in agreement with those reported by Conway and Ellis [14], namely a decrease in arterial pressure secondary to a fall in cardiac output without significant change in SVR. The increase in heart rate is a baroreceptor-mediated reflex response to the decrease in arterial pressure. The increased heart rate, coupled with direct myocardial depression and decreased preload secondary to reduced venous tone, resulted in a significant decrease in stroke volume. The administration of vecuronium had no observable effect on the trends in cardiovascular parameters, confirming it as an appropriate choice of muscle relaxant for this type of investigation.

It is more difficult to compare our results for the response to laryngoscopy and intubation with those reported by other workers because the available studies have used a variety of patient groups (e.g. geriatric patients, patients with peripheral vascular disease and patients taking cardiovascularly active drugs) and differing induction agents [14–17]. However, all available studies indicate increases in SVR between 30 and 90 s after intubation, although changes in cardiac output were neither consistent nor statistically significant. The one study comparable to ours is that by Vohra *et al.* [18] who used identical measurement techniques (NCCOM3 and Dinamap) to compare the response to thiopentone and propofol in healthy female patients. Although their induction sequence differed from ours in that intubation was performed 90 s after induction (when haemodynamic parameters are still changing rapidly), their findings in patients induced with thiopentone are very similar to those presented here.

The pressor response and tachycardia following laryngoscopy and intubation are associated with an increase in SVR and a reduction in stroke volume. The tachycardia is β-adrenoceptor mediated, and may be attenuated by β-blockade [2, 19, 20]; the increase in SVR is α-mediated and results from increased plasma concentrations of noradrenaline [21]. β-adrenoceptor blockade has no effect on this response [19]. Our measurements show that despite the increased sympathetic drive during intubation, the accompanying tachycardia is coupled with a reduction in SV. Thus, cardiac output shows little change. In the absence of transient myocardial depression or reduction in preload, the reduced stroke volume is secondary to the substantial increase in afterload caused by the elevated SVR.

Besides offering a convenient noninvasive method for observing rapid variations in cardiac output in response to drug administration or other stimuli, TEB is applicable in studying large numbers of patients under routine clinical conditions. By investigating such samples of patients, we will be able to obtain reliable estimates of the population response to the sequence of induction, laryngoscopy and intubation. Although all three premedication groups show comparable mean results, there is wide interindividual variability of response (as reflected by wide 5th to 95th centile ranges). Moreover, for those variables with statistically significant changes from baseline, the ranges of the centile limits do not embrace zero change, despite their non-gaussian distribution. Thus if the BoMed and noninvasive blood pressure measurements are used to compare the effects of different anaesthetic agents or to investigate the responses to anaesthesia in patients with cardiovascular disease, the results are unlikely to be subject to type I errors. However, small sample populations should not be relied upon if the aim is to detect small yet clinically significant changes with a high degree of accuracy; large populations will compensate both for interindividual variability and the variability of the machinery used. Provided that the anaesthetist is looking for changes greater than the reproducibility of the various noninvasive techniques, then their use may allow data to be obtained from healthy patients where invasive monitoring techniques cannot be justified ethically.

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Vecuronium: an anthropometric comparison

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Summary

This study set out to determine if there was any resistance to vecuronium in Nepalese studied in Nepal compared with Nepalese, Chinese and European patients studied in Hong Kong. The four groups, each of 10 male and 10 female patients, were intubated 60 s after administration of 0.1 mg.kg^{-1} vecuronium. The Nepalese patients in Nepal had significantly less satisfactory intubating conditions ($p = 0.002$). Similarly, male patients had significantly less satisfactory conditions than female patients ($p = 0.004$). Some anthropometric measurements were significantly different between the patients in Nepal and those in Hong Kong. There were also sex-related anthropometric differences. It is suggested that differences in response to vecuronium could be explained by differences in distribution volume and muscle mass

Key words

Neuromuscular relaxants; vecuronium.
Genetic factors; race.

Although genetic variation causing differences in drug metabolism is well recognised [1], little work has been done on the effect of race or geography on muscle relaxants, other than the incidence of cholinesterase variants [2]. However, Katz *et al.* noted that the durations of action and magnitude of neuromuscular blockade of suxamethonium and tubocurarine were prolonged in Americans compared with the British [3]. This transatlantic difference was also found in USAF servicemen stationed in the UK. Levy [4], in a pharmacokinetic analysis of Katz's data and also that of Walts and Dillon [5] who had investigated the interaction of tubocurarine and suxamethonium in Los Angeles, suggested that the transatlantic differences with suxamethonium could be explained by a slower elimination in the New York population compared with those in Los Angeles or the UK. On a visit to Nepal on Operation Nightingale [6] to help with earthquake relief at the British Military Hospital in Dharan (Nepal), the anthropometric differences between the Nepalese living in Nepal and the Nepalese soldiers and their families serving in Hong Kong (Ghurkas) were very obvious. It was therefore decided to extend an ethnic comparison of vecuronium in the three groups of patients encountered in Hong Kong military medical practice, namely Nepalese, Chinese and European to include a study of the indigenous Nepalese in eastern Nepal.

Methods

The study received ethics committee approval from the Army Medical Research Executive and the Research Ethics Committee of the Chinese University of Hong Kong and all patients gave written consent. There were 20 healthy adult patients (aged 18–55 years) in each group, namely indigenous Nepalese in Nepal, (NN); Ghurka soldiers (recruited in Nepal) and their dependents (Nepalese) posted to Hong Kong, (NH); indigenous Hong Kong Chinese soldiers, their dependants and civilians locally employed by the Ministry of Defence in Hong Kong, (CH) and, British servicemen, United Kingdom based civil servants and their dependants posted to Hong Kong, (EH).

There were equal numbers of male and female patients in each group, who were selected consecutively from those scheduled for elective surgery where tracheal intubation using antidepolarising muscle relaxants was indicated. Those with known hepatic or renal disease were not studied. Anaemia did not debar patients from being included in the Nepal part of the study.

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Table 1. Assessment of intubation by ethnic group.

Relaxation of jaw	Relaxation of vocal cords	Overall assessment
Excellent	Excellent (widely abducted)	Excellent (no reaction)
Satisfactory	Satisfactory (slight movement of cords on intubation)	Satisfactory (slight movement or bucking)
Fair	Fair (moderate movement of cords, cough on intubation)	Fair (moderate movement or bucking)
Poor	Poor (cords adducted and held)	Poor (intubation impossible)

All the anaesthetics (including the intubations) were given by the same anaesthetist (I.T.H) and comparable anaesthetic equipment and drugs were used in all cases. All patients received a standard anaesthetic. Premedication was with oral diazepam given approximately 1 h before the estimated time of surgery. Those weighing under 45 kg received 5 mg, those between 45 and 70 kg 10 mg, and those over 70 kg 15 mg. Anaesthesia was induced with thiopentone in a dose not exceeding 5 $mg.kg^{-1}$ body weight, given over approximately 20 s until loss of verbal response, and vecuronium (0.1 $mg.kg^{-1}$) was given immediately following. Intubation was attempted at exactly 60 s following the end of the injection of vecuronium and was assessed according to the scale in Table 1. The anaesthetics and assessment were carried out by the same anaesthetist (I.T.H.).

Where the intubating conditions were poor or impossible, a further attempt was made 30 s later, at 90 s after injection of the vecuronium. If intubation was still difficult, another attempt was made 30 s later at 120 s. An increment of vecuronium (0.05 $mg.kg^{-1}$) was given after this to facilitate intubation, if required. A Magill folding laryngoscope with an adult Macintosh blade was used for the intubations with a Magill oral polyvinyl tracheal tube (Portex Ltd) of appropriate size. Anaesthesia was maintained with 70% nitrous oxide in oxygen plus enflurane 1.0–2.0% and was administered with a continuous flow anaesthesia machine using a coaxial breathing attachment. The lungs of all patients were mechanically ventilated, the ventilation being adjusted to keep the end-tidal concentration of carbon dioxide between 4.5 and 5.5 kPa. Neuromuscular function was monitored and further vecuronium (1–2 mg) was given as needed. The time and dose were recorded. At the end of surgery, the neuromuscular block was antagonised with neostigmine mixed with atropine.

For the purpose of statistical analysis, grading of intubation at 60 s was categorised into satisfactory (excellent and satisfactory) and unsatisfactory (fair and poor).

The patients' age, height, weight, skinfold thickness over the triceps and subscapular muscles and arm circumference were noted pre-operatively. All the skinfold thicknesses were measured with the same Lange skinfold calipers by the same investigator. Mean arm muscle circumference was calculated from the formula:

Arm muscle circumference = Arm circumference − (3.14 × triceps skinfold) with all measurements in centimetres. Ideal anthropometric measurements were taken from Blackburn and colleagues [7].

Haemoglobin and biochemical tests for hepatic and renal functions were carried out in the respective laboratory where the patients were located. Pulse and blood pressure were recorded using a noninvasive automatic recorder (Dinamap). Neuromuscular block of the ulnar nerve supplying the *m. abductor digiti minimi* was monitored with an anaesthesia and brain activity monitor (Datex, ABM) in Hong Kong and with a functionally similar neuromuscular transmission monitor (Datex, Relaxograph) in Nepal. Full relaxation was defined as $t_1 = 0\%$. The hand and wrist were splinted and the forearm kept warm with a heat reflecting blanket. Oxygen and carbon dioxide concentrations in the circuit were measured with a carbon dioxide and oxygen analyser (Datex CD 102) in both locations.

Analysis of variance was used for anthropometric data, drug dose and relaxant times, and Chi-squared tests for intubation data. For statistical analyses $p < 0.05$ was considered significant. All data are expressed as mean (SD) unless specified otherwise.

Results

Patient details and their demographic values (Table 2) show that the indigenous Nepalese (NN) are generally lighter and slimmer than the Nepalese, Chinese and Europeans in Hong Kong, although only the Europeans are significantly taller than the other groups.

Eighty-five percent of patients in the NN group had unsatisfactory intubating conditions after the administration of vecuronium, whereas only 20% had unsatisfactory intubating conditions in the NH group. The proportion of satisfactory to unsatisfactory intubating conditions in the CH group (40%:60%) and the EH group (50%) were approximately equal. The differences were significant between the NN and the other groups ($p = 0.002$) using contingency table analysis and Chi-squared test (Fig. 1). The individual p values between groups were:

	NH	CH	EH
NN	0.001	> 0.05	0.020
NH	—	0.004	0.048
CH	—	—	> 0.05

Following the administration of vecuronium, the times to full relaxation were shorter in the NN and EH groups than those in the NH and CH groups (Table 3). The duration of full relaxation in the NN group was shorter than the other three groups. None of these differences was statistically significant.

The mean doses of thiopentone used were NN 4.55 (0.48) NH 4.21 (0.09) CH 4.30 (0.42) EH 4.13 (0.72) $mg.kg^{-1}$. The

Table 2. Demographic data by ethnic group and sex. Values are expressed as mean (SD).

Group	NN	NH	CH	EH	All groups
Mean age; years					
Combined	38.2 (11.8)*	29.2 (5.1)	33.4 (6.3)	34.1 (8.9)	33.7 (9.0)
Male	37.9 (11.3)	31.8 (5.2)	31.1 (4.8)	31.5 (8.8)	33.1 (8.5)
Female	38.5 (12.2)	26.5 (3.5)	35.7 (6.8)	36.6 (8.2)	34.3 (9.5)
Mean height; m					
Combined	1.56 (0.08)	1.59 (0.06)	1.63 (0.09)	1.71 (0.12)*	1.62 (0.11)
Male	1.61 (0.05)	1.64 (0.03)	1.70 (0.06)	1.81 (0.09)	1.69 (0.10)
Female	1.51 (0.08)	1.53 (0.03)	1.56 (0.04)	1.62 (0.07)	1.56 (0.07)
Mean weight; kg					
Combined	50.0 (7.7)*	63.0 (11.2)	60.2 (11.3)	73.3 (14.7)*	61.6 (14.2)
Male	49.7 (6.8)	67.6 (7.0)	68.2 (6.5)	78.5 (12.2)	66.0 (13.4)
Female	50.2 (8.4)	58.5 (12.6)	52.3 (9.4)	68.0 (15.0)	57.2 (13.6)
% ideal weight					
Combined	89.7 (14.5)	109.6 (18.2)	100.0 (14.3)	110.3 (21.8)	102.4 (19.3)
Male	81.6 (11.0)	107.5 (9.3)	101.9 (9.5)	104.1 (12.7)	98.7 (14.7)
Female	97.8 (12.9)	111.8 (23.7)	98.0 (17.6)	116.5 (26.6)	106.0 (22.5)
Triceps skinfold; mm					
Combined	9.18 (4.54)*	13.98 (5.84)	14.05 (6.23)	13.79 (6.44)	12.75 (6.16)
Male	6.13 (2.12)	10.82 (3.92)	10.32 (3.10)	9.70 (2.57)	9.24 (3.52)
Female	12.23 (4.26)	17.14 (5.73)	17.77 (6.35)	17.88 (6.55)	16.26 (6.24)
Subscapular skinfold; mm					
Combined	11.24 (4.83)*	17.13 (8.23)	17.17 (6.24)	15.67 (7.19)	15.30 (7.16)
Male	9.13 (4.08)	13.78 (5.53)	14.42 (4.20)	13.05 (3.57)	12.60 (4.86)
Female	13.34 (4.60)	20.47 (9.08)	19.92 (6.72)	18.29 (8.77)	18.01 (8.02)
Mid arm circumference; mm					
Combined	239.8 (33.4)*	276.0 (42.2)	280.9 (33.1)	304.8 (42.7)	275.4 (44.7)
Male	232.5 (36.9)	288.5 (18.5)	290.0 (15.3)	312.0 (27.1)	280.8 (39.1)
Female	247.0 (27.7)	263.5 (54.0)	271.8 (42.3)	297.5 (53.2)	270.0 (49.0)
Arm muscle circumference; mm					
Combined	210.9 (27.8)*	232.1 (39.0)	236.8 (29.2)	261.4 (38.9)	235.3 (38.6)
Male	213.2 (32.6)	254.5 (10.6)	257.6 (11.6)	281.5 (22.2)	251.7 (32.4)
Female	208.6 (21.8)	209.6 (43.8)	216.0 (26.7)	241.3 (41.6)	218.9 (37.2)
% standard arm muscle circumference					
Combined	87.1 (11.6)	95.5 (14.6)	97.4 (9.8)	107.6 (14.6)	96.9 (14.7)
Male	84.3 (12.9)	100.6 (4.2)	101.8 (4.6)	111.3 (8.8)	99.5 (12.8)
Female	89.9 (9.4)	90.4 (18.9)	93.1 (11.5)	104.0 (17.9)	94.3 (16.0)
Surface area; m^2					
Combined	1.47 (0.13)	1.64 (0.15)	1.64 (0.18)	1.85 (0.23)	1.65 (0.22)
Male	1.50 (0.10)	1.73 (0.14)	1.79 (0.10)	1.98 (0.19)	1.75 (0.18)
Female	1.44 (0.14)	1.55 (0.14)	1.49 (0.11)	1.72 (0.19)	1.55 (0.21)

For explanation of abbreviations see Legend to Figure 1.
*represents difference is significant compared with all other groups ($p < 0.05$).

percentage of smokers in the groups were NN 30%, NH 10%, CH 15% and EH 50%.

Liver function tests were within normal limits in all four groups of patients, although the mean total bilirubin level in the NN group was 17.1 (2.1) $mol.l^{-1}$ compared with 14.4 (11.0) $mol.l^{-1}$ in the NH group, 11.2 $mol.l^{-1}$ in the CH group and 10.2 $mol.l^{-1}$ in the EH group. The mean haemoglobin level of 12.7 $g.100\ ml^{-1}$ (two patients having values of less than 10 $g.100\ ml^{-1}$) in the NN group was significantly lower than the range of 14.1–14.3 (1.4) $g.100\ ml^{-1}$ in the other groups ($p < 0.05$). Gamma glutamyl transferase was 29.7 (22.6) IU in NH, 20.7 (11.0) IU in CH, and 30.4 (25.6) IU in EH.

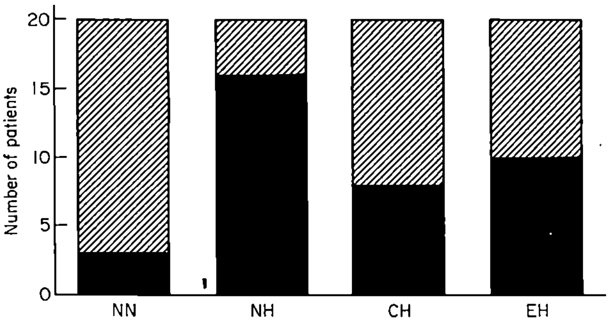

Fig. 1. Ease of intubation by ethnic group at 60 s. ■, satisfactory; ▨, unsatisfactory; NN, indigenous Nepalese in Nepal; NH, Ghurka soldiers and their dependants posted to Hong Kong; CH, indigenous Hong Kong Chinese soldiers, their dependants, and civilians employed by the Ministry of Defence; EH, British servicemen, UK based civil servants and dependants posted to Hong Kong.

The data were further analysed by sex grouping. The women had significantly larger mean triceps and subscapular skinfold thicknesses, but their mean arm muscle circumference was less, being 94% of ideal (female) compared to 99% of ideal (male) for men (Table 2). The men had a mean percentage of ideal weight of 99 (15%) compared with the women's 106 (22%). The mean thiopentone dose was 4.26 $mg.kg^{-1}$ for males and 4.18 $mg.kg^{-1}$ for females. The ease of intubation conditions is displayed diagrammatically by race and sex in Figure 2. The females had better intubating conditions at 60 s after vecuronium ($p < 0.004$). There was no difference in either the time to full relaxation or the duration of relaxation between males and females (Table 4).

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Table 3. Muscle relaxation. Time to reach full relaxation and duration of full relaxation by ethnic group. Values are expressed as mean (SD).

Group	NN	NH	CH	EH
Time to full relaxation; min	3.9 (0.8)	4.4 (1.5)	4.7 (0.6)	3.8 (1.5)
Duration of full relaxation; min	16.8 (6.9)	21.2 (7.6)	20.8 (6.6)	23.5 (10.4)

For explanation of abbreviations see legend to Figure 1.

Table 4. Muscle relaxation. Time to reach full relaxation and duration of full relaxation by sex. Values are expressed as mean (SD).

	NN	NH	CH	EH	All groups
Time to full relaxation; min					
Male	3.86 (0.87)	3.75 (0.78)	4.50 (0.41)	4.05 (1.59)	4.03 (1.06)
Female	3.91 (0.73)	5.10 (1.66)	4.95 (0.65)	3.55 (1.17)	4.40 (1.32)
Duration of full relaxation; min					
Male	14.4 (4.0)	23.2 (8.6)	23.3 (7.3)	20.9 (6.2)	20.4 (7.7)
Female	19.2 (7.8)	19.2 (5.4)	18.9 (4.6)	26.1 (12.4)	20.0 (8.7)

For explanation of abbreviations see legend to Figure 1.

Thirty percent of males smoked compared to only 23% of the females.

Discussion

This study shows that the Nepalese patients living in Nepal had less satisfactory intubating conditions at 60 s following the administration of vecuronium compared with Nepalese and other ethnic patients in Hong Kong.

Our method of assessment was based on a study of intubation conditions by Clarke and Mirakhur [8]. Their assessment of intubations at 60 s after a dose of vecuronium 0.1 mg.kg^{-1} appeared to be a good combination to investigate and compare the sensitivity to vecuronium. It was impossible for observers to be blind, but we had a single assessor (I.T.H.) together with another observer in order to minimise the interobserver bias. We feel that our assessment is comparable with Clarke's study: we saw a similar percentage of patients with satisfactory intubating conditions in our European and Chinese patients (50% European and 40% Chinese versus 40% in Clarke's patients), whereas in the Nepalese patients, 80% in the Hong Kong (NH) group were satisfactory but only 15% in the Nepal (NN) group which, as is suggested later, may be the result of differences in muscle mass and in the distribution volume of the muscle relaxant.

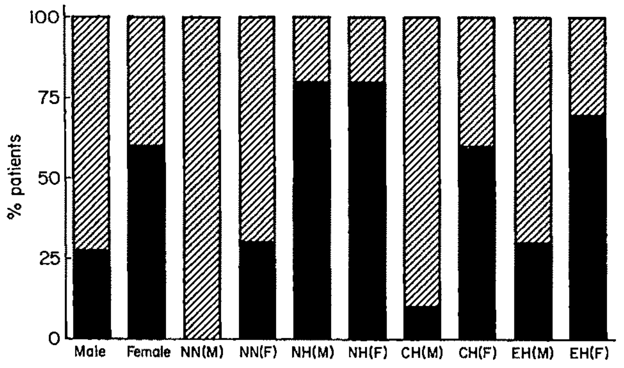

Fig. 2. Ease of intubation by sex at 60 s. ■, satisfactory; ▨, unsatisfactory. Abbreviations as for Figure 1 and (M), male; (F) female.

Ease of tracheal intubation depends upon the degree of muscular relaxation, depth of anaesthesia and technical proficiency [9]. We measured neuromuscular transmission to the *m. abductor digiti minimi* electromyographically [10]; there were no intergroup differences in the time to reach 100% block of neuromuscular transmission (4.2 (1.2) min). Casson and Jones [11] showed, with a dose of vecuronium 0.1 mg.kg^{-1}, a latent onset time of 74 (19) s and a manifest onset time of 85 (27) s. Agoston [12], Kreig and co-workers [13], and Mirakhur [14] have suggested that vecuronium produces complete relaxation of the vocal cords when the hand muscles are only about 50% paralysed. It is possible that we may have accomplished intubation before the muscle relaxant was effective, but Clarke in his study had observed that intubating conditions after thiopentone could not be related to the onset of neuromuscular blockade [8]. Young, Clarke and Dundee [15] have suggested that thiopentone in a dose of 5 mg.kg^{-1} produces sufficient jaw relaxation to permit laryngoscopy. The mean dose of thiopentone required in our study was less than 5 mg.kg^{-1} in all the groups, although the Nepalese in Nepal (NN) were found to have received more thiopentone on a weight basis than the other groups.

Goat and colleagues [16] showed that the speed of muscle paralysis after injection of a muscle relaxant depended on muscle blood flow; and as tissue perfusion is inversely related to blood viscosity, alterations in blood viscosity may affect onset time [17]. Although patients in Nepal had a lower mean haemoglobin value, they had less satisfactory intubating conditions, which suggests that their anaemia did not significantly enhance the speed of onset of the muscle relaxant.

Duvaldestin and Henzel showed that only 30% of vecuronium is bound to plasma proteins, mainly to albumen [18] and therefore the modest alterations in protein binding with age, sex, oral contraceptives and cyesis are unlikely to be associated with clinically important effects. The lower mean concentration of albumen in the NN group, which is within the normal clinical range, was unlikely to affect the action of vecuronium. We had equal numbers of males and females in the groups; none of the women were pregnant.

The Nepalese studied in Nepal were significantly older but none was older than 53 years and therefore this is unlikely to be of clinical significance. d'Hollander and colleagues could show no difference in the sensitivity to vecuronium between patients aged less than 40 and those aged 40–60 years [19].

The patient's lungs were ventilated with 1% enflurane in nitrous oxide and oxygen prior to intubation. Enflurane can potentiate vecuronium [20], but in the short time of less than 60 s before intubation it was unlikely to produce significant individual differences. There was no difference between mean onset time and mean duration of vecuronium between the males and females, but the women had significantly better intubating conditions. Thus, better intubating conditions were found both in women and in patients living in Hong Kong. This is similar to what Donati and Bevan [21] found in women with pancuronium, that the onset time of muscle relaxation was shorter, and they suggested that this could have been due to differences in distribution volume and body composition.

Differences in sensitivity to muscle relaxants have been demonstrated in paediatric patients, with nondepolarising muscle relaxant requirements being age dependent. Meretoja [22] suggests that the more rapid effect of muscle relaxants in neonates and infants can be explained by changes in sensitivity, distribution volume and muscle mass. Extracellular fluid volume mirrors the distribution volume of muscle relaxants, but whilst this cannot be the sole explanation for any differences, changes in the body composition during growth could be the reason, because of the major changes in the fat and muscle compartments after the age of one year [23]. No changes in sensitivity would be expected in adult patients but there are sex differences in muscle mass and there may have been a difference in distribution volume, with those living in Nepal having lower mean weights and skinfold thicknesses. A larger dose of muscle relaxant is needed when there is less fat and more muscle [22], a factor common to both males and the Nepalese in Nepal (NN).

Katz and others compared the effects of tubocurarine and suxamethonium in patients in London (UK) and New York (USA) and found that the magnitude and duration of action of tubocurarine was less in patients living in London than in New York [3]. He then went on to study American servicemen stationed in England and found that they responded similar to patients in New York. In our study, we also found a geographical difference, but unlike Katz's Americans, our Nepalese have altered their response on settling in Hong Kong. Although no anthropometric data were available on Katz's patients, it is unlikely that American servicemen would have changed their standard of living with their ready access to the PX (military shopping facility for US sourced goods) and USAF Commissary (US Air Force facility for US sourced groceries, vegetables and meat) and therefore they would not have altered their anthropometric measurements significantly. In contrast, Nepal is a poor country with a very low standard of living and those who are recruited into the British Army become relatively wealthy and receive adequate nutrition, unlike the indigenous population. The increase in mean body weight, mean triceps skinfold thickness and mean arm muscle circumference of the NH group compared with the NN group suggests a considerable increase in both fat and muscle bulk in the NH group. This could well affect the pharmacokinetics of vecuronium and hence the different response to vecuronium observed. Unfortunately, we were unable to determine the pharmacokinetics of vecuronium because of a lack of the necessary logistic facilities in Nepal.

In conclusion, this study has suggested that anthropometric factors are associated with differences in the effect of vecuronium on early intubation. The need for different countries to undertake their own research into the effects of drugs on their own populations is borne out by this study. Further work on the influence of anthropometry on other muscle relaxants is suggested.

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Implicit memory tested in children during inhalation anaesthesia

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Summary

Memory for stimuli presented during inhalation anaesthesia was tested in 80 children undergoing eye surgery. Two groups were exposed, in a random double-blind study, to repeated neutral phrases including either the colour orange or green. A postoperative colouring task was used as a test of implicit memory to detect any preference for the colour named under anaesthesia. No colour preference attributable to implicit memory could be demonstrated. One patient had a distinct preference for the named colour. No patient remembered any intra-operative events.

Key words

Anaesthesia; paediatric.
Anaesthetics, volatile; halothane.
Memory.

Patients under general anaesthesia may 'hear' if tests of implicit memory are used to test perception during the anaesthetised state. Until recently, memory tests were restricted to explicit tasks (recall, recognition) with few, if any, positive results. Tests of implicit memory [1,2] do not, in contrast with explicit tasks, refer to a learning episode, but refer to a change in task performance as compared with a control group. Amnesic patients, who by definition show poor recall, do not show similar impairment of memory when implicit memory is tested [3].

Word stem completion is one of the several tests of implicit memory. Words are presented in an initial learning phase, and in the test phase, the first three letters of each word are given, and the subjects are asked to complete the stem with the first word that comes to mind. An effect is assumed when presented words are substituted more frequently than nonpresented words. Eich, Reeves and Katz [4] tested implicit memory under general anaesthesia and found no effect, whereas a strong effect was seen by our own group [5] under isoflurane anaesthesia. These findings were repeated when a balanced anaesthetic technique was used [6], while other groups either found similar results [7–9], or found no evidence of an effect [10,11].

The present study was designed to investigate memory storage under general anaesthesia by using an adapted test of implicit memory in young children undergoing eye surgery. We opted for the repeated verbal presentation during anaesthesia of a neutral sentence, emphasising the name of a colour. It was expected that children would demonstrate implicit memory of the colour by showing a preference for the colour in the postoperative phase.

Methods

Eighty patients were scheduled for paediatric strabismus surgery under general anaesthesia. The study was approved by the medical ethics committee of the University Hospital of Leiden and 44 patients were operated on for the first time; 36 had had previous operations. Patients with no command of the native language were not studied, nor were those with hearing difficulties and learning or psychiatric disorders. Forty-eight patients were female and 32 were male aged between 4 and 11 years (mean 5.95, SD 2). All were ASA 1 or 2. Parental, and where appropriate, the child's consent was asked and three refused to participate.

The patients were allocated in a random, double-blind manner to two groups. Both received 20 repeated recordings, via identical tapes and headphones, of the sentence '*the child is playing with the orange/green ball*' (group O, orange; group G, green). The particular colours were chosen because a preliminary study had shown that although they were familiar to the children, neither were favourites.

All the stimuli were presented for 10 min about 15 min before end of general anaesthesia, at the same stage of surgery. The time was chosen to standardise as much as

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possible the amount of anaesthetic administered after the stimulus. A neutral sound was played before and after the stimulus (the sound of birds singing).

The morning after operation the patients were presented with a colouring picture of a child playing with a multifaceted beach ball. Six coloured pencils were offered in a randomised set. The patient was invited to select a colour for each of the eight facets in turn, and to name each colour as it was selected. The colouring was done by the experimenter. The order of the named colours was noted, and the picture given to the child to complete and keep. The experimenter then checked that the child knew the colours by name, and asked about the operation to test for any explicit recall. Children who did not know the exact name of all the colours were retained in the study. Where there was a discrepancy we used the named colour rather than the actual colour of the pencil chosen.

Anaesthesia

Premedication of oral trimeprazine 4 mg.kg^{-1} was given 2 h before operation. In children above 40 kg (n = 6) this was substituted with oral temazepam 10 mg. The children were pre-oxygenated for 2 min, and anaesthesia was induced either by inhalation with halothane (59) or by intravenous thiopentone (21). Suxamethonium 1 mg.kg^{-1} was used for tracheal intubation. In all patients anaesthesia was maintained with oxygen 33% in nitrous oxide 67% and an additional inhalational agent. Halothane was used in all except two patients, one of whom received isoflurane, the other enflurane. In 61 patients end-tidal concentrations were measured using a Normac (Datex) and maintained between 1.0 and 3.5%.

The results are expressed as mean (SD). For both colours, preference scores were assigned to each child based on the position of the experimental colour in the row of successively named colours. Thus preference for the correct colour in the first facet scored 8, in the second 7 and so forth. This gave a possible maximum of 36, should a child have chosen the experimental colour for all the facets. Scores for both colours for all the children were subjected to a one way ANOVA with the group colour as the independent variable.

Results

Duration of operation was 54.2 (10.7) min, and the delay between the stimulus and the postoperative test was 22.1 (2) h. For O and G groups, the minimum end expiratory inhalation agent concentrations were 1.7% (n = 31 range 1–2.7%) and 1.7% (n = 30 range 1.3–2.6%) respectively, and the maximum concentrations were 1.89% (n = 31 range 1.2–2.9%) and 1.9% (n = 30 range 1.4–2.6%), during the test period.

In the postoperative tests, 71 out of 80 children were able correctly to identify the names of the different colours used. None had any recall of hearing anything during surgery. The distributions for the first colour choices in each group are shown in Table 1.

Orange scores were 5.1 (2.5) and 4.86 (2.2) and green scores were 5.55 (2.9) and 6.10 (2.9) for the O and G groups respectively. No significant differences were found between groups (for orange F = 0.18 DF = 1,78 p = 0.67; for green F = 0.71 DF = 1,78 p = 0.4).

Table 1. Distribution of first choices for the different colours in the colouring task, for the two groups (O = Orange; G = Green).

	Group	
	O	G
Blue	5	5
Yellow	4	13
Red	9	5
Purple	13	6
Orange	6	3
Green	3	8

Six patients in the O group selected orange as their first choice, and eight in the G group selected green as their first choice. When these 14 'hit' cases were compared with the rest of the sample with respect to all the variables measured no significant differences were found.

Discussion

We were unable to detect any implicit memory in children undergoing eye surgery under inhalation anaesthesia. Studies in which postoperative motor responses were prompted by intra-operative suggestion have also failed to demonstrate an effect, but it is difficult to determine whether these are tests of implicit memory.

Few studies of memory under anaesthesia have been conducted in children, and none has used tests of implicit memory. Recall and dreaming were studied in 202 patients aged 7 to 14 years using various anaesthetic techniques [12]. Recall of intra-operative events was reported in 5% of the patients, and 6% reported dreams. In another study [13] 41 children between 5 and 13 years received a combination of general and regional anaesthesia. They received either 1.5 or 0.5% halothane. Twenty patients with uncontrolled halothane anaesthesia acted as controls. The patients in the two test groups received 'well known words' during surgery. After operation, patients in the 0.5% halothane group recalled significantly more 'correct' words than in the 1.5% group, although neither group differed from the blank control group. In 373 children, between 5 and 17 years, none reported recall [14] although 19% reported dreams. Of those who received suxamethonium, 24% had dreams compared with 9% who received atracurium. A prospective study in 144 children aged 5–14 years undergoing day case surgery, and in which suxamethonium was used, compared pretreatment with d-tubocurarine with no pretreatment [15]. Dreaming occurred in 2.8% of the first group and in 16.7% of the latter. There was no spontaneous recall. The incidence of awareness in children appears to be low [16], although dreaming seems to occur frequently in children who are anaesthetised.

The discrepancy between this study and our earlier work may be explained by the fact that in this study the work was on children. Tests of implicit memory, which are vulnerable to changes in the modality studied [17], are based on the activation or strengthening of existing memory representations [18]. In children, and particularly in young children, these may not have been fully developed, and activation of memory may be less developed. The use of trimeprazine as a premedicant may also have influenced results.

In the previous studies, the positive results were found shortly after anaesthesia [5,6,8], whereas the studies which found negative results were those which tested several days later [4,10]. Those which tested with an intermediate delay (1–2 days) yielded intermediate results [7,9]. No studies have addressed which anaesthetic agent was used, and this must be studied. Halothane may, for pharmacodynamic reasons, have prevented memory activation [19].

The parents of one of the children reported a preference in their child after the operation for the colour orange. They were curious to know which colour their child had been exposed to. It was orange. She had chosen orange as her first colouring task. Another child reported anxiety, and voices telling her that she would die. This could not be associated with the study.

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Catecholamine response to laryngoscopy and intubation

The influence of three different drug combinations commonly used for induction of anaesthesia

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Summary

The haemodynamic response and changes in plasma catecholamine concentrations associated with laryngoscopy and tracheal intubation were compared during anaesthesia employing three strictly standardised techniques with commonly used drug combinations. Thirty-six patients were investigated consecutively resulting in 12 patients in each of three study groups. Anaesthesia was induced with thiopentone 5 mg.kg^{-1} (group 1), fentanyl 6 μg.kg^{-1} with thiopentone 5 mg.kg^{-1} (group 2), or midazolam 0.2 mg.kg^{-1} with fentanyl 6 μg.kg^{-1} (group 3). Undesirable changes in haemodynamic effects and an elevation of plasma catecholamine concentrations during laryngoscopy and intubation occurred in group 1. Heart rate and mean arterial pressure increased significantly (34% and 23% respectively). Noradrenaline concentration increased by a maximum of 147%. The addition of fentanyl (groups 2 and 3) attenuated the adverse haemodynamic response and elevation of plasma catecholamine concentrations; heart rate and mean arterial pressure did not differ from pre-intubation values and plasma catecholamine concentrations decreased steadily. Substitution of thiopentone by midazolam in combination with fentanyl abolished the adverse haemodynamic response and modified the increase in plasma catecholamine concentrations. 'High-dose' opioid anaesthesia is not necessary to produce optimal conditions during laryngoscopy and intubation.

Key words

Sympathetic nervous system; catecholamines.
Intubation, tracheal; complications.
Anaesthetics, intravenous; thiopentone, midazolam.

The sequence of induction of anaesthesia, laryngoscopy and tracheal intubation is associated with marked haemodynamic changes and autonomic reflex activity, and may be a cause of concern in many high risk patients [1–3].

A diversity of results exists about protective measures against haemodynamic and catecholamine responses to laryngoscopy and intubation, but no single anaesthetic technique has become generally accepted as being effective in preventing or attenuating these responses [3]. Measurements of plasma catecholamines have been used to monitor overt changes in sympathetic activity and several studies have reported increases in plasma concentrations of noradrenaline following laryngoscopy irrespective of measures taken to prevent them [4–8].

However, the design of many previous catecholamine studies makes data interpretation difficult. Premedication has differed within and between study groups, which have included patients of different ages, and dosages of anaesthetics and the time interval between drug administration and laryngoscopy were often not standardised. A number of studies are flawed by difficulties with the methodology of catecholamine assay.

Considering the diversity of catecholamine results, our aim was to investigate changes in plasma catecholamine concentrations during induction of anaesthesia, including laryngoscopy and tracheal intubation, with three commonly used drug combinations. The depression of adrenergic activity during laryngoscopy and intubation may be considered as advantageous in the clinical management of patients with coronary artery disease. Before investigating patients with cardiovascular diseases it was our intention to study homogeneous groups of healthy subjects. Our laboratory has developed a valid assay for measurement of plasma catecholamine concentrations [9, 10].

In our study, we used either thiopentone or midazolam to provide the hypnotic component of a balanced anaesthetic technique. Thiopentone was selected because it continues to be the most popular anaesthetic induction agent worldwide [11] and midazolam because it is the benzodiazepine of choice for use in anaesthetic induction [12].

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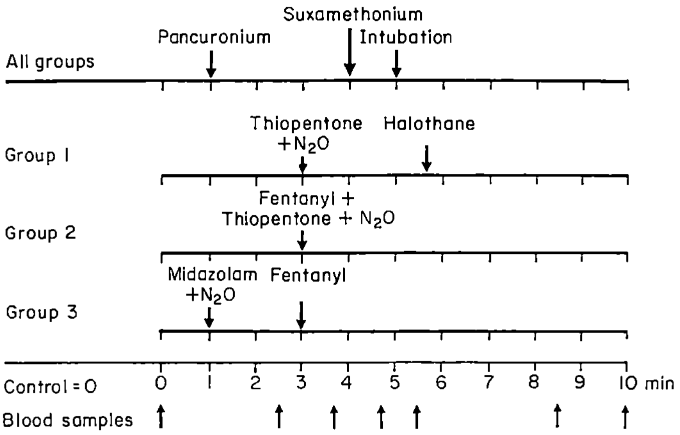

Fig. 1. Time line describing the various interventions and data collection points during the study.

Thiopentone (alone or with fentanyl 0.1 mg) does not protect against the increase in sympathetic activity imposed by laryngoscopy and tracheal intubation [13, 14]. Kautto [15] has shown that thiopentone with fentanyl 6 μg.kg^{-1} completely abolishes the tachycardic and hypertensive response to intubation, although plasma catecholamine concentrations were not measured.

Midazolam alone is able to produce a decrease of sympathetic activity [16] although it does not block the haemodynamic stress of tracheal intubation [17]. Midazolam with fentanyl 5–7.5 μg.kg^{-1} [18] blocked the tachycardia and hypertension secondary to intubation, but again plasma catecholamine concentrations were not measured. Boralessa *et al.* [19] concluded, in terms of the response to laryngoscopy, that midazolam provided a relatively stable cardiovascular system during induction of anaesthesia and in this respect was superior to thiopentone. Thus, the combination of midazolam and fentanyl might influence plasma catecholamine concentration changes associated with laryngoscopy and intubation. Consequently, the drugs and drug combinations we investigated for induction were: thiopentone alone; fentanyl plus thiopentone; and midazolam plus fentanyl. The drugs were used in dosages recommended in the literature and given under strictly standardised conditions.

Patients and methods

After approval by the Copenhagen County Scientific Ethics Committee and informed consent, 36 patients (ASA class 1) scheduled for elective minor orthopaedic or gynaecological surgery were studied. The patients comprised three groups with 12 patients in each, studied consecutively. The study was finished within 8 weeks using a carefully standardised technique. None of the patients was receiving any chronic medication.

On the morning of surgery, a central venous catheter for blood sampling was inserted via an antecubital vein after application of local anaesthesia without adrenaline. Oral premedication of diazepam 0.3 mg.kg^{-1} was given, and 60 min later, patients were transported to the anaesthetic room. Immediately before induction of anaesthesia, a baseline blood sample was collected for measurement of plasma concentrations of catecholamines: noradrenaline, adrenaline, and dopamine. An intravenous line for fluid and drug administration was inserted in the ipsilateral arm. On the contralateral arm, arterial pressure and pulse rate were recorded every min by an automatic monitoring device (Dinamap 1846 (Critikon)). Electrocardiogram (ECG) lead V_5 was recorded continuously by a strip-chart recorder during the 10-min study period. After induction of anaesthesia, the lungs were ventilated with a modified Mapleson D breathing system. Ventilation was adjusted to maintain end-tidal carbon dioxide concentration at 4.5 to 5.0% (Normocap, Datex). Laryngoscopy was performed with a normal MacIntosh blade. Rüsch tracheal tubes of internal diameter 7.0 mm for women and 8.0 mm for men were used. Tracheal intubation was performed by the same trained anaesthetist in all patients.

The procedure in each of the three study groups is demonstrated in Figure 1. Induction of anaesthesia, laryngoscopy and tracheal intubation were performed under strictly standardised conditions. All patients received a precurarising dose of pancuronium 0.015 mg.kg^{-1}. Anaesthesia was induced in group 1 by thiopentone 5 mg.kg^{-1} over 15 s, in group 2 by fentanyl 6 μg.kg^{-1} as a bolus plus thiopentone 5 mg.kg^{-1} over 15 s, and in group 3 by midazolam 0.2 mg.kg^{-1} over 15 s followed 2 min later by fentanyl 6 μg.kg^{-1} as a bolus. Anaesthesia was maintained in all patients by 67% nitrous oxide in oxygen. Three minutes after administration of pancuronium, all patients received suxamethonium 1.5 mg.kg^{-1}, and the trachea was intubated 1 min later. Anaesthesia was supplemented with halothane 2% 40 s after intubation in group 1.

Blood samples were taken in a strictly systematised manner for measurement of plasma catecholamine concentrations (Fig. 1). The first 5 ml were discarded before the sample of 10 ml was drawn. Plasma concentrations of noradrenaline, adrenaline and dopamine were determined using radio-enzymatic labelling and high pressure liquid chromatographic separation [9]. In our laboratory, the ranges of normal venous concentrations for noradrenaline are 0.4 to 1.9 (mean 0.92) nmol.l^{-1}, for adrenaline 0.07 to 0.32 (mean 0.16) nmol.l^{-1}, and for dopamine 0.31 to 0.67 (mean 0.50) nmol.l^{-1}. Within the range of normal values, the coefficients of variation were 6% for noradrenaline, 14% for adrenaline, and 10% for dopamine. Sensitivity of the assay was 0.07 nmol.l^{-1} for noradrenaline and adrenaline, and 0.18 nmol.l^{-1} for dopamine [10].

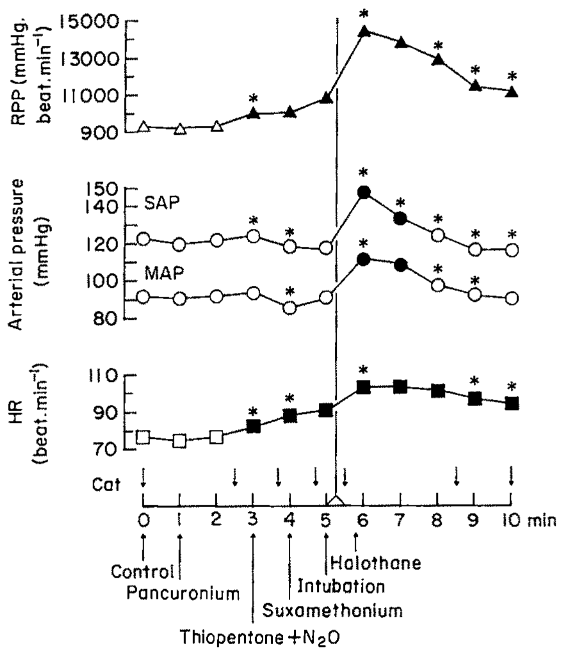

Fig. 2. Relationships between rate-pressure product (RPP), systolic arterial pressure (SAP), mean arterial pressure (MAP), and heart rate (HR) in Group 1. Closed symbols indicate statistically significant changes from awake control values. Stars indicate statistically significant changes from preceding value. Arrows above the abscissa indicate time for blood sampling for assessment of plasma catecholamine concentrations (CAT). Median values are shown. For further explanation see text.

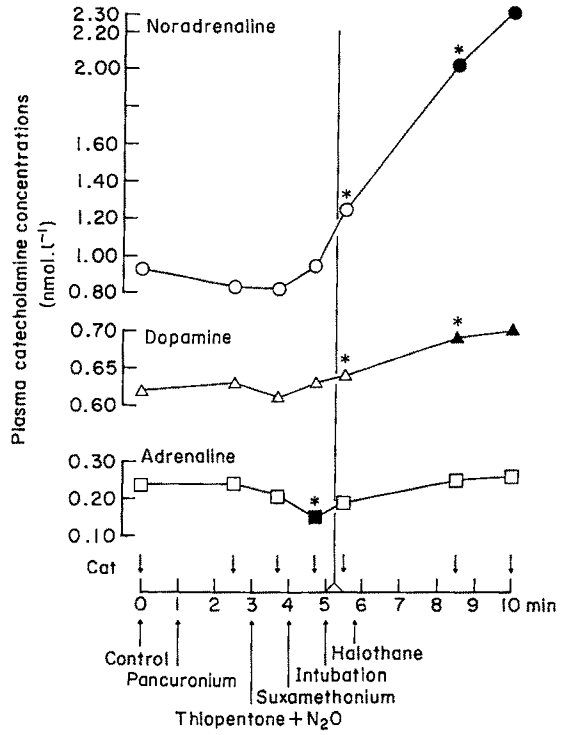

Fig. 3. Relationships between plasma concentrations of noradrenaline, dopamine, and adrenaline in Group 1. Blood samples were drawn from the central venous site. Closed symbols indicate statistically significant changes from awake control values. Stars indicate statistically significant changes from preceding value. Arrows above the abscissa indicate time for blood sampling for assessment of plasma catecholamine concentrations (CAT). Median values are shown. For further explanation see text.

Blood samples for measurement of plasma fentanyl concentrations by radio-immunoassay in groups 2 and 3 were drawn immediately before fentanyl administration and 40, 100, 150, and 420 s after the bolus injection of fentanyl [20].

Nonparametric statistics were used throughout because of the small number of patients.

Results are given as median and range. Statistical analysis included a Friedman test of variance followed by a Wilcoxon test for evaluation of paired differences within groups, or a Mann-Whitney test for differences between groups. The degree of association between corresponding haemodynamic and catecholamine data was evaluated by computing the Spearman rank correlation coefficient (r_s). In all cases, $p < 0.05$ was considered statistically significant.

Results

The groups were comparable with regard to age, weight, sex ratio, and surgery. The median (range) age was 35 (18–51) years in group 1, 35 (20–49) years in group 2, and 28 (21–41) years in group 3. The median (range) values of weight were 68 (45–80) kg, 64 (55–106) kg, 75 (60–100) kg, and the sex ratios (m:f) were 5:7, 4:8, and 6:6, in groups 1, 2 and 3 respectively.

Induction of anaesthesia, laryngoscopy and intubation

In *group 1*, heart rate increased by 9% after administration of pancuronium (Fig. 2), and continued to increase after administration of thiopentone and suxamethonium. Laryngoscopy caused a further increase in heart rate. This increase was statistically significant compared to both the pre-induction (34%) and the preceding values (13%). Five minutes after laryngoscopy, and 4 min after beginning halothane inhalation, heart rate was still 22% higher than before induction. The systolic and mean arterial pressures remained unchanged during induction, whereas laryngoscopy was followed by significant increases in each (26% and 23% respectively), lasting less than 3 min.

The rate-pressure product (RPP) increased gradually by 16% during induction, but an increase of 55% took place 1 min after laryngoscopy; RPP exceeded 12 000 in 11 of 12 patients.

The plasma noradrenaline concentration was unchanged initially during induction (Fig. 3). After laryngoscopy, there was a 32% increase. The increase continued during halothane administration and reached a maximum of 147% 5 min after laryngoscopy (compared to the pre-induction value). The plasma adrenaline concentration decreased by 38% after induction but returned to the pre-induction value a few minutes after laryngoscopy. The plasma dopamine concentration increased by 13% after laryngoscopy and administration of halothane.

In *group 2*, heart rate increased significantly by 7% after pancuronium (Fig. 4), and remained at this level after the administration of fentanyl, thiopentone, and suxamethonium, until recovery 2 min after laryngoscopy. The systolic and mean arterial pressures decreased steadily during the entire period without increases after laryngoscopy and intubation. RPP was not influenced by laryngoscopy.

The plasma noradrenaline, adrenaline, and dopamine concentrations showed steady and gradual decreases by 39%, 56% and 8% respectively (Fig. 5).

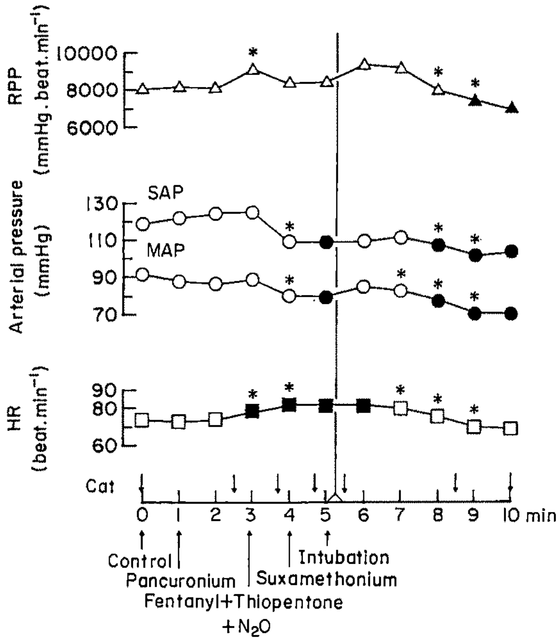

Fig. 4. Group 2 See legend to Figure 2.

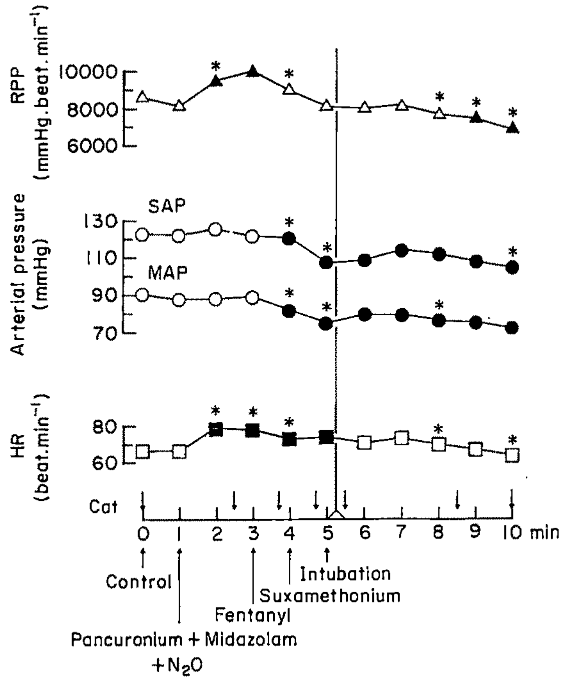

Fig. 6. Group 3 See legend to Figure 2.

In *group 3,* heart rate increased by 18% after administration of pancuronium and midazolam (Fig. 6), but decreased somewhat after administration of fentanyl. Heart rate after laryngoscopy was not significantly different from the pre-induction value. The systolic and mean arterial pressures decreased by 13% and 18% after induction and remained lower than pre-induction values even after laryngoscopy.

A statistically significant increase (16%) in RPP occurred during induction. The highest value appeared 2 min after administration of pancuronium and midazolam. However, RPP 1 min after laryngoscopy was not different from the pre-induction value.

The plasma noradrenaline concentration decreased by 48% during induction (Fig. 7), with an increase towards the pre-induction value 30 s after laryngoscopy. The plasma adrenaline concentration was reduced by 65% during induction and remained low after laryngoscopy. Plasma dopamine concentration increased significantly with laryngoscopy.

Comparison between groups

Pre-induction heart rates and arterial pressures were similar in the three groups. The increases in heart rate and arterial pressure after laryngoscopy in group 1 did not occur in groups 2 and 3, and we could not demonstrate any differences in haemodynamic values between those groups. The differences between group 1 and groups 2 and 3 with regard

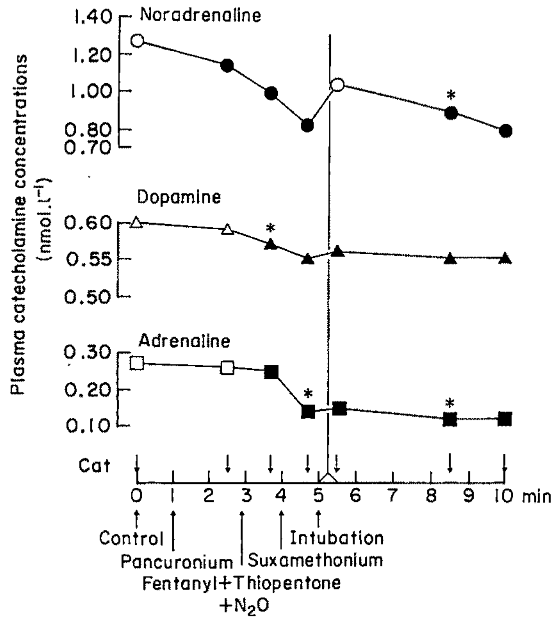

Fig. 5. Group 2 See legend to Figure 3.

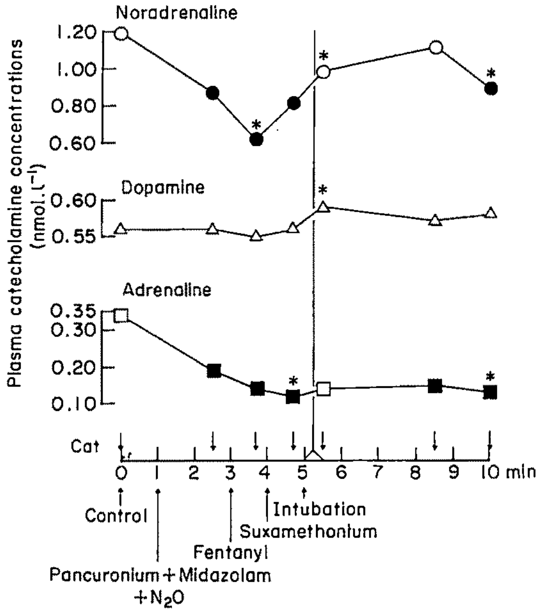

Fig. 7. Group 3 See legend to Figure 3.

Table 1. Median (range) plasma concentrations of fentanyl (ng.ml^{-1}) achieved after administration of a bolus dose of fentanyl 6 μg.kg^{-1} at time: 0.

Time (s)	Group 2	Group 3
0	ND	ND
40	17.3 (7.3–209.0)	24.5 (6.8–167.0)
100	7.0* (2.4–10.7)	9.2* (4.1–33.2)
150	5.1 (1.5–7.0)	5.9 (3.6–9.2)
420	2.9 (1.0–3.7)	3.3 (2.0–4.3)

ND, not detectable.
*$p < 0.05$ between groups.
Tracheal intubation was performed at time: 120 s.

to RPP just before and immediately after laryngoscopy were statistically significant. In groups 2 and 3, RPP exceeded 12 000 in only one patient (12218) following laryngoscopy; in group 1 this occurred in 11 of 12 patients.

The large increase in noradrenaline concentration in group 1 after laryngoscopy and intubation was not present in groups 2 and 3, which had similar catecholamine patterns without statistically significant differences. However, noradrenaline and dopamine concentrations increased significantly in group 3 when post-laryngoscopy values were compared with values immediately before laryngoscopy.

A statistically significant correlation between RPP and plasma noradrenaline concentration was found in group 1, but significant correlations did not exist between cardiovascular and catecholamine data in group 2 or 3.

The plasma fentanyl concentrations in groups 2 and 3 are shown in Table 1. The values just before laryngoscopy (7.0 and 9.2 ng.ml^{-1} respectively) differed significantly ($p < 0.05$).

Discussion

Our study showed that a potentially harmful cardiovascular response was elicited by laryngoscopy and tracheal intubation after induction of anaesthesia with thiopentone and suxamethonium (group 1). The reason for the increases in heart rate and arterial pressure is probably related to sympathetic stimulation caused by laryngoscopy [13]. In our patients, this stimulation was suggested by the abrupt increase in plasma noradrenaline concentration observed immediately after laryngoscopy. Although thiopentone has been demonstrated to decrease sympathetic activity and to reduce baroreceptor sensitivity in unstimulated patients [21, 22], our results are in agreement with recent findings that thiopentone 4 mg.kg^{-1} in combination with a neuromuscular blocking agent does not prevent marked haemodynamic stimulation and activation of the sympathetic nervous system provoked by laryngoscopy and intubation [13, 14].

Pancuronium has been demonstrated experimentally to increase plasma noradrenaline concentrations by blocking noradrenaline re-uptake in nerve synapses [23]. However, this action may be dose-dependent (or without measurable clinical significance) because induction of anaesthesia which included pancuronium 0.1 mg.kg^{-1} was not accompanied by increased sympathomimetic activity [5]. When administered in precurarising doses as in the present study, no change in plasma catecholamine concentrations was found, and the increase in heart rate we observed after pancuronium is thus attributed to its vagolytic activity. Suxamethonium apparently had no effect of its own on cardiovascular function or catecholamine concentrations, and this is in accordance with previous findings [3, 5, 14]. In our view, the frequent observation in group 1 of RPP values exceeding 12 000 after laryngoscopy and intubation, occurring in more than 90% of these healthy patients, makes induction with pancuronium, thiopentone (without fentanyl) and suxamethonium an inadvisable procedure, especially in patients with an increased risk of myocardial ischaemia. We are aware, however, that RPP is not a precise indicator of myocardial oxygenation in the anaesthetised patient.

High-dose fentanyl ($> 50\ \mu$g.kg^{-1}) is claimed to produce 'stress-free anaesthesia', and both the pressor and the catecholamine responses to laryngoscopy are abolished [3]. Preloading with a moderate to low dose of fentanyl ($< 10\ \mu$g.kg^{-1}) has also been demonstrated to attenuate the haemodynamic reaction to laryngoscopy, although to a lesser degree [3, 15, 24]. A bolus injection of fentanyl 6 μg.kg^{-1} given exactly 2 min before laryngoscopy and intubation in our patients prevented the haemodynamic stimulation and nearly abolished the catecholamine activation.

As demonstrated for thiopentone, induction of anaesthesia with midazolam also resulted in a transient depression of baroreceptor reflex function and a sustained decrease in catecholamine concentrations [16]. When thiopentone and midazolam were compared in patients anaesthetised for cardiac surgery, midazolam was found to attenuate the hypertensive response to laryngoscopy to a greater extent than thiopentone [19]. However, in elderly patients in whom anaesthesia was induced with either thiopentone or midazolam, both a hypertensive reaction and increases in plasma catecholamine concentration were induced by laryngoscopy [25]. We found that fentanyl 6 μg.kg^{-1}, in combination with either thiopentone or midazolam, attenuated the hypertensive/tachycardic response and the catecholamine release following laryngoscopy to almost the same extent.

The variability reported on the effects of a low dose of fentanyl on the response to laryngoscopy may be related to the dosage and timing of fentanyl administration in relation to laryngoscopy. Fentanyl is eliminated rapidly from plasma and 99% of the dose administered is concentrated in tissues within 5 min; the brain, lung and heart concentrations reach their maximum within 30 s of an injection [26]. As fentanyl elimination follows a multicompartment model, redistribution between tissues takes place within the first minutes after injection. In patients anaesthetised with oxygen–fentanyl, an average plasma fentanyl concentration of 15–25 ng.ml^{-1} was adequate to secure haemodynamic stability during laryngoscopy and intubation [27, 28], whereas concentrations lower than 9 ng.ml^{-1} may allow patients to become responsive to stimuli. Thus, the protective effect of a low dose of fentanyl (as part of anaesthetic induction) may depend on both the inhibition of plasma catecholamines induced by the concomitant administration of a hypnotic agent and the timing of drug administration before laryngoscopy. When fentanyl 5 μg.kg^{-1} was administered over 5 min (1 μg.kg.min^{-1}) in a rapid sequence induction with thiopentone (2 mg.kg^{-1}) and suxamethonium, Cork *et al.* [24] found significantly lower heart rates and arterial pressures after laryngoscopy than in control patients given thiopentone 4 mg.kg^{-1} and no fentanyl. Although a statistically significant increase in plasma noradrenaline concentration was found in the control group but not in the fentanyl group after laryngoscopy, absolute plasma catecholamine concentrations did not differ between groups. The noradrenaline increase in the fentanyl group was not statistically significant after laryngoscopy due to a huge patient-to-patient variability in the noradrenaline baseline value of 413 ± 1560 pg.ml^{-1} (mean ± 2 SD). A general tendency towards great patient-to-patient variability in plasma catecholamine concentrations in the study of Cork *et al.* may be explained partly by the fact that they drew samples from a peripheral forearm vein and partly because they investigated rather inhomogeneous groups of patients (some with hypertension needing medication). In a pilot study with patients who received fentanyl from 1 to 6 min before intubation, we found that the maximum protective effect against the hypertensive and tachycardic reaction to laryngoscopy obtained by fentanyl 6 μg.kg^{-1} in combination with thiopentone was seen when fentanyl was administered as a bolus exactly 2 min before laryngoscopy. However, the plasma fentanyl concentrations achieved in our patients suggest that the maximum effect of this dosage was achieved 1–2 min after its administration.

Previous studies regarding the effect of halothane on plasma catecholamine concentrations have produced conflicting results as both an increase and decrease in plasma noradrenaline have been demonstrated following halothane administration [3, 7, 29, 30]. Our results are in accordance with previous findings that halothane administration leads to a significant increase in catecholamines, especially noradrenaline [7, 30]. The increase induced by halothane in our study was even higher than that caused by laryngoscopy. The noradrenaline response was not correlated to any change in heart rate or arterial pressure and it thus seemed to be an effect of halothane itself. A pronounced plasma catecholamine rise in response to sudden administration of halothane 2% may have some significance with respect to arrhythmias and sensitisation of the myocardium to exogenous catecholamine administration seen during halothane anaesthesia [31–33].

Although conditions were highly standardised it is a drawback that the subjects in our study were not randomised. The investigation was planned and carried out as three separate consecutive studies. The details of the anaesthetic techniques chosen for groups 2 and 3 were first decided after the results of group 1 and groups 1 and 2 respectively were known. However, the investigation was performed over a very short period of time without changes in patient population and types of surgery, but because random allocation was not used, we found it inappropriate to combine data provided in Figures 2, 4 and 6, and 3, 5 and 7.

In conclusion, undesirable and potentially harmful haemodynamic effects combined with elevation of plasma catecholamine concentrations occurred in response to laryngoscopy and tracheal intubation after thiopentone and suxamethonium, with an even greater increase in plasma noradrenaline and dopamine concentrations following halothane administration. The addition of a bolus dose of fentanyl 6 μg.kg^{-1} 2 min before intubation and the omission of halothane significantly attenuated the increase in circulatory and catecholamine stimulation. Substitution of thiopentone by midazolam similarly abolished the haemodynamic stimulation and to some extent also depressed the catecholamine reaction.

'High-dose' opioid anaesthesia is not necessary to produce optimal conditions during laryngoscopy and intubation.

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Opioid sensitivity of chronic pain: a patient-controlled analgesia method

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Summary

Twenty-two patients with chronic pain of malignant or nonmalignant origin were given intravenous morphine by patient-controlled analgesia. A prestudy judgment was made from the characteristics of the pain as to whether it was nociceptive or neuropathic. Analgesic efficacy was assessed by a nurse-observer; adverse events were noted and plasma morphine and metabolitie concentrations measured. Three categories of opioid response were distinguished. Good responders obtained > 70 mm relief on the visual analogue scale, with minimal or manageable adverse events. Moderate responders obtained < 70 but > 30 mm relief with more problematic adverse events, and poor responders had < 30 mm relief with troublesome adverse events. This method for the study of opioid sensitivity allowed a wide dosage range to be studied. The simultaneous analgesic and adverse event measurements showed that the spectrum of observed response was wide, and response category could be judged for the majority by 4 h. In those with poor or moderate response, adverse event severity limited further dose increment. The relationship between pain characteristics and response showed that some pains judged to be neuropathic had a good response to opioid (5/13), and some pains judged to be nociceptive did not (5/14). The study suggests that the pattern of response is not as black and white as the prediction of good response from nociceptive pain and poor from neuropathic pain would suggest, although nociceptive pain was more likely than neuropathic pain to show a good response. For the moderate responders opioid titration may, in the absence of other effective treatments, be useful, but the analgesic endpoint may not be totally satisfactory. The method provides an operational definition of opioid sensitivity.

Key words

Pain; chronic.
Opioid administration; patient controlled analgesia.

There is a considerable controversy as to whether or not all pains are sensitive to opioids [1]. Clinically the intensity of an opioid sensitive pain shows substantial reduction with an adequate dose of opioid, and an insensitive pain does not. A more precise definition of sensitivity would be the demonstration of a valid dose-response for analgesia with increasing opioid dose. The extremes of the controversy are on the one hand that some pains are opioid insensitive [2], and on the other that opioid sensitivity is a relative rather than an absolute phenomenon [3]. Neuropathic pain, pain associated with disease or dysfunction of the nervous system, is thought particularly to be associated with opioid insensitivity [2]. Three of the central questions in the controversy are: does opioid insensitivity exist? If so, is it a relative rather than an absolute phenomenon? Are certain clinical pain syndromes predictive of different degrees of opioid sensitivity?

The concept of decreased opioid sensitivity came from clinical observation. Confirmation under controlled conditions presents considerable methodological difficulties, outlined below. A significant problem has been the absence of an animal model which shows loss of opioid sensitivity. An increase rather than a decrease in opioid sensitivity has been a feature of chronic 'inflammatory' pain models [4]. Allodynia produced by ischaemic spinal cord injury did, however, show reduced sensitivity to systemic morphine 24–48 h after the injury [5]. A lack of animal pain models with decreased opioid sensitivity could be construed as showing that reduced opioid sensitivity is not a real phenomenon. An alternative view is that the mechanism or timescale of the models, or both, is not an adequate representation of what is observed clinically; this emphasises the need to develop adequate methods for investigation of the problem in patients.

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Three categories of clinical study may be distinguished. In the first, patients with neuropathic pain were given small bolus increments of morphine by injection to a maximum of 20 or 30 mg; dose-dependent analgesia and the ability of naloxone to reverse the analgesia were noted [6]. More recently repeated boluses of morphine to a maximum of 0.3 $mg.kg^{-1}$ has been used [7]. In the second, infusions of opioid were used for patients with neuropathic, nociceptive or idiopathic pain, and the analgesic effects were recorded. The maximum doses used were 20 mg of morphine given intravenously over 15 min [2]. In the third type of study an infusion with the option of higher opioid doses was used, and analgesia and adverse events were recorded [3]. An infusion method was also employed in a study of post-herpetic neuralgia [8]. At least three important variables: the range of opioid doses tested, the previous opioid exposure of the patients, and the endpoints, analgesia alone or analgesia plus adverse events, have to be considered, and each of these three study types has limitations with regard to one or more of these variables.

The issue of the range of dose tested in these studies is crucial. Some of the patients studied will have had previous exposure to opioids, and may therefore need doses higher than the 'usually effective' doses tested. The dose-response is shifted to the right relative to the dose-response for an opioid-naive patient. False-negative results could thus occur if response is sought only at a single dose. The change in the analgesic response to morphine with previous opioid exposure was well shown [9]. Even in the absence of previous opioid exposure, if opioid sensitivity is a relative rather than an absolute phenomenon, imposition of dose limits may again produce false-negative results with regard to analgesia.

This study is an attempt to use patient-controlled analgesia (PCA) to improve the clinical investigation of opioid sensitivity. Chronic pain patients with nociceptive, neuropathic, idiopathic or both nociceptive and neuropathic types of pain used PCA with a single opioid, morphine, with simultaneous nurse observer measurement of analgesia and adverse events, and with measurements of plasma morphine concentration. The putative advantage of PCA is that, unlike the methods used previously to study this problem, it allows the patient to use as much morphine as necessary to achieve the desired outcome, analgesia. The nurse observer measurement of analgesia and adverse events provides an analgesic outcome measure independent of the PCA, and provides adverse event information.

Methods

Patients

Ethical approval was obtained for the study. Informed consent was sought, with general practitioner approval, from patients of either sex with either chronic nonmalignant pain or chronic cancer-related pain, unresolved by other interventions or unrelieved by nonopioid analgesics or with poor pain relief on existing or previous opioid regimens. They had to be alert and communicative, and be able to comprehend PCA and the assessment scales. If the patient was taking a relatively long-acting opioid, such as morphine as a sustained release formulation or buprenorphine, these drugs were stopped at least 3 days before starting PCA, and were replaced by the equivalent dose of morphine sulphate as solution. All analgesics were withheld for at least 3 h before the study.

Patient-controlled analgesia

The PCA device used was a PRODAC [10]; the syringe driver contained 5 ml of a 10 $mg.ml^{-1}$ solution of morphine sulphate connected via extension tubing to an intravenous cannula in the arm. The machine was set up with a bolus size of 0.05 ml, with no lockout period. The latency between button pressing and completion of dose delivery was less than 1 min. Maximum dosage rates built in to the programme allowed no more than 0.5 ml in any 1 min period, 1 ml in any 5 min period and no more than 3 ml in any 60 min period. Neither loading bolus nor background infusion were used. The concentration of morphine sulphate was increased if necessary to 15 or 30 $mg.ml^{-1}$.

All the subjects had current pain intensity rated as moderate or severe (see below) before the study. If they had received opioids overnight, PCA was started only when they were experiencing no relief (verbal categorical scale for pain relief = 0) from the last dose. PCA was started between 0830 and 1000 h, and the aim was to maintain it for 24 h. The study was stopped before 24 h only if it was considered clinically unsafe to keep the patient on PCA or if the patient decided to withdraw.

Instructions

The patients were told that the main aim of the PCA was to see how effective morphine was in relieving their pain(s), and that they were going to be responsible for their own analgesia for 24 h. They were taught how to use the hand-held button before connection to the PCA device. The patients were encouraged to ask as many questions as necessary to understand both machine and the study. If they were concerned about adverse events they were reassured that there would be close medical and nursing supervision, and that they could discontinue whenever they wished. As soon as the machine was connected they were told: 'You are in charge now, so try to make yourself pain-free'.

Assessments

A clinical judgement as to whether the pains were nociceptive, neuropathic or idiopathic was made before starting PCA. The pains were judged to be nociceptive if there was a proven pathological process related to the painful area but no neurological abnormality; neuropathic if there was a proven pathological process related to the painful area and somatosensory dysfunction could be demonstrated and idiopathic if there was no demonstrable organic pathology to account for the pain [2]. If any patient had pain at more than one site, the pains at each site were evaluated separately.

All assessments were made by one nurse observer. The timing of the various recordings is shown in Table 1. The following scales were used: *Pain intensity: during PCA the patient was asked: 'How bad is your pain at the moment?'* This was answered on (a) a 4-point categorical verbal rating scale (none = 0, mild = 1, moderate = 2 and severe = 3); (b) an 8-point randomised categorical scale (Tursky words, no pain = 0, just noticeable = 1, weak = 2,

Table 1. Timing of recordings and samples.

		During PCA (h)				
	Before PCA	2	4	6	8	24
Pain intensity						
4 point categorical	+	+	+	+	+	+
8 word	+	+	+	+	+	+
VAS	+	+	+	+	+	+
McGill questionnaire	+					+
Pain relief						
5 point categorical	+	+	+	+	+	+
VAS	+	+	+	+	+	+
Mood	+	+	+	+	+	+
Side effects	+	+	+	+	+	+
Plasma samples	+	+	+	+	+	+

mild = 3, moderate = 4, strong = 5, severe = 6 and excruciating = 7); (c) a 100 mm visual analogue scale (VAS pain intensity, 'No pain' at one end and 'Worst possible pain' at the other). *Pain relief: during PCA the patient was asked: 'How much pain relief have you got at the moment from the morphine?'* This was answered on (a) a 5-point categorical verbal rating scale (none = 0, slight = 1, moderate = 2, good = 3 and complete = 4); (b) an 100 mm visual analogue scale (VAS pain relief (VASPR), 'No relief of pain' at one end and 'Complete relief of pain' at the other).

A 100 mm visual analogue scale (VAS) was used to measure mood, 'Best I could feel' at one end and 'Worst I could feel' at the other, while the McGill pain questionnaire recorded the number of words chosen and sum rank scores.

Adverse events

Volunteered adverse events were recorded at the times shown in Table 1. The patient was asked: 'is morphine upsetting you in any way at the moment?' or 'do you have any adverse event now?' Observed adverse events were also recorded, with emphasis on level of consciousness and respiratory rate. A 4-point categorical verbal rating scale (none = 0, mild = 1, moderate = 2 and severe = 3) was used to rate the severity of each adverse event reported.

If the volunteered adverse events included nausea and/or vomiting, metoclopramide 10 mg was given intravenously and repeated after 2 h. If no control was achieved, either prochlorperazine 12.5 mg by deep intramuscular injection or haloperidol 1.5 mg orally was given. If with those interventions nausea and/or vomiting could be controlled, it was considered manageable, and if not as unmanageable.

Other adverse events such as confusion, lack of concentration, drowsiness, itching, dry mouth or sweating were not treated actively. If any of these adverse events were present the patient was asked to say whether they were acceptable or unacceptable ('can you put up with it or not?'). If the adverse event was rated unacceptable, the patient was asked if they wished to continue on PCA.

Blood sampling and analysis

From an intravenous cannula in the other arm, blood samples were taken at the times shown in Table 1, and the cumulative dose of morphine delivered was recorded at the same time. Samples were centrifuged, the plasma separated and stored frozen until analysis. Morphine (Coat-a-Count, DPC, Los Angeles) and morphine-3-glucuronide (M3G) were measured using a differential radioimmunoassay technique. The ratio of M3G to morphine (M3G:M ratio) was calculated. Plasma creatinine, aspartate-aminotransferase (AST), total bilirubin and alkaline phosphatase (ALP) were measured by standard laboratory techniques. Renal dysfunction was defined as plasma creatinine concentration higher than 150 μmol.l^{-1}. Hepatic dysfunction was defined as results on at least two of the three liver function tests higher than the upper limit of normal for the hospital laboratory (total bilirubin: 3–17 μmol.l^{-1}, AST: 15–42 iu.l^{-1}, ALP: 80–250 iu.l^{-1}).

Statistical analysis

The Mann–Whitney *U*-test was used where appropriate. Statistical significance was assumed where probabilities were less than 0.05.

Results

Patient details

Twenty-two patients were studied, five male and 17 female. The average age was 52 years (range 23–78). Sixteen patients had pain at a single site (judged clinically to be nociceptive in nine cases, neuropathic in six and idiopathic in one patient). Six patients had pain at two sites (two pains): both were considered as neuropathic in three patients, both as nociceptive in two patients and in one patient the pain at one site was judged to be neuropathic and at the other nociceptive (Table 2). No patient had hepatic or renal dysfunction. Thirteen of the 22 patients completed 24 h on PCA and nine were withdrawn because of unacceptable adverse events (see below and Table 2).

Analgesic response

Twelve patients had an analgesic response judged as good. The basis of the 'good' judgement was the VAS pain relief score, which was greater than 70 mm at more than one assessment time (Fig. 1). Nine patients (Nos. 2, 5, 8, 9, 11, 14, 15, 21, 22) obtained this degree of relief at the first assessment and continued with the same degree of relief during most of the time on PCA. Three patients (Nos. 1, 13, 19) did not obtain this degree of relief at the first assessment, but achieved it subsequently (Fig. 1). Of the 13 patients with a good response, 10 (Nos. 1, 2, 5, 8, 9, 11, 13, 14, 21, 22) obtained complete analgesia, a score of four on the categorical scale for pain relief or 100 mm on VAS pain relief, at at least one assessment time during PCA.

Five patients (Nos. 7, 10, 17, 18, 20) had a poor analgesic response to PCA (Fig. 2). Patient 7 was unable to complete the VAS scales because of adverse events, and no figure for this patient is presented. The basis of the 'poor' judgement was the VAS pain relief score, which was not greater than 30 mm at more than one assessment time. Three of these five patients had experienced morphine adverse events which were sufficiently severe that they were unable to complete the VAS scales; despite this they were still complaining of severe or moderate pain. The main adverse event was severe drowsiness. Patients 7 and 10 were rous-

Table 2. Patient details.

					Before study					Study			
Patient	Sex	Age; years	Diagnosis	Pain; No.	Clinical judgement	Opioid regimen	Last dose to PCA; h	Pain intensity; mm	McGill score	Time on PCA; h	Morphine dose on PCA; mg	Response	Antiemetic interventions
1	F	78	Rheumatoid arthritis	1	Nociceptive	DPP 97.5 mg by mouth 4 times a day	10	80	32	24	48.6	Good	0
2	M	74	Abdominal 2° (unknown 1°)	1	Nociceptive	No	—	52	22	24	17.0	Good	0
3	F	44	Multiple sclerosis	2	Neuropathic Neuropathic	No	—	91 91	51 51	24	38.5	Moderate Moderate	4
4	M	23	Paraplegia L1	2	Neuropathic Neuropathic	No	—	52 77	29 15	24	52.2	Good Moderate	3
5	F	49	Multiple sclerosis	1	Neuropathic	MSS 40 mg by mouth 4 times a day	9	98	35	24	70.6	Good	0
6	F	46	Arachnoiditis	2	Neuropathic Neuropathic	DHC 60 mg by mouth twice a day	3.5	95 95	57 52	24	76.2	Moderate Moderate	2
7	F	75	Arachnoiditis	1	Neuropathic	No	—	100	71	2.5	53.7	Poor	2
8	F	24	Chronic pancreatitis	1	Nociceptive	PE 200 mg by mouth 3-hourly	5	88	25	24	83.2	Good	2
9	M	23	Chronic pancreatitis	1	Nociceptive	PE 100 mg by mouth 4-hourly	5	68	18	24	137.0	Good	2
10	F	54	Rheumatoid arthritis	2	Nociceptive Nociceptive	DHC 120 mg by mouth 2-hourly	3.5	78 83	28 28	5	133.7	Poor Poor	2
11	F	48	Arachnoiditis	1	Nociceptive	No	—	62	55	24	36.7	Good	4
12	F	68	Perineal pain	1	Idiopathic	DPP 65 mg by mouth once daily	192	85	48	6.25	36.7	Moderate	2
13	F	75	Breast cancer	1	Nociceptive	DHC 30 mg by mouth 4-hourly	10	45	15	24	70.6	Good	1
14	F	52	Colorectal cancer	1	Nociceptive	DHC 30–120 mg.day^{-1}	30	53	40	6	35.7	Good	1
15	F	42	Breast cancer	1	Neuropathic	MSS 40 mg 4-hourly and 80 mg at night	10.5	60	17	24	297.7	Good	0
16	M	58	Post-thoracotomy	1	Neuropathic	PE 50 mg by mouth 4 times a day — DPP 65 mg by mouth 4 times a day	6 72	81	27	6.5	91.0	Moderate	1
17	F	54	Vater's ampulla cancer	1	Nociceptive	DM 30 mg SC 4-hourly	8.5	95	53	7	342.9	Poor	1
18	F	46	Arachnoiditis	1	Neuropathic	DHC 30 mg by mouth three times a day	192	97	38	2.8	46.6	Poor	2
19	F	44	Abdominal scar and back pain	2	Neuropathic Nociceptive	MSS 20 mg 4-hourly	10	91 96	58 58	22.8	122.3	Good Good	0
20	F	48	Lung cancer	2	Nociceptive Nociceptive	MSS 30 mg 4-hourly	13	55 90	36 40	4	74.4	Poor Poor	0
21	M	57	Mesothelioma right lung	1	Neuropathic	MMS 40 mg 4-hourly	8	68	26	24	149.7	Good	0
22	F	66	Cancer of the cervix	1	Nociceptive	DPP 65 mg 4–5 times a day	11.5	96	39	24	39.3	Good	3
Total					14 Nociceptive 13 Neuropathic 1 Idiopathic							14 Good 7 Moderate 7 Poor	

DPP, dextropropoxyphene; MSS, morphine sulphate solution; DHC, dihydrocodeine; PE, pethidine; DM, diamorphine.

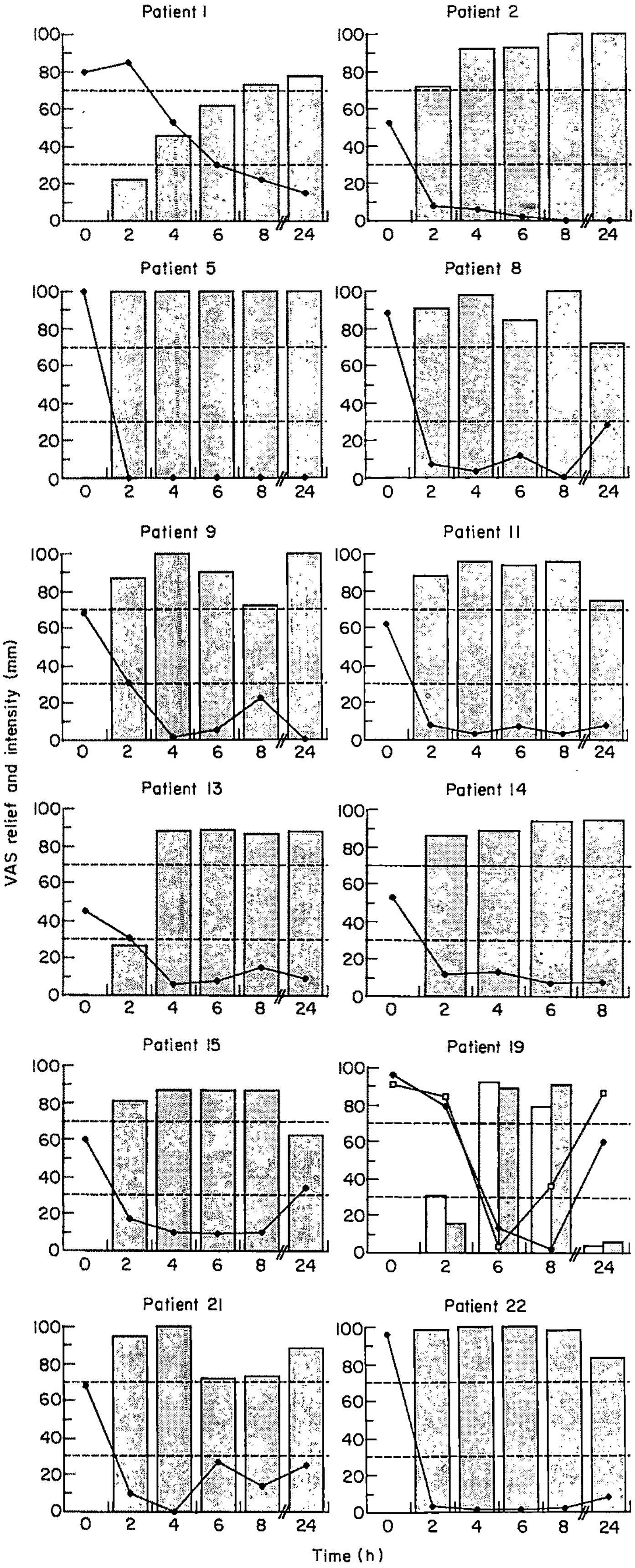

Fig. 1. Individual patients' analgesic response while taking PCA for those patients with 'good' response (VAS pain relief score greater than 70 mm at more than one assessment time). Time (h) on the x-axis; VAS (mm) pain relief (columns) and pain intensity (lines) on the y-axes. Patient 19 had two pains.

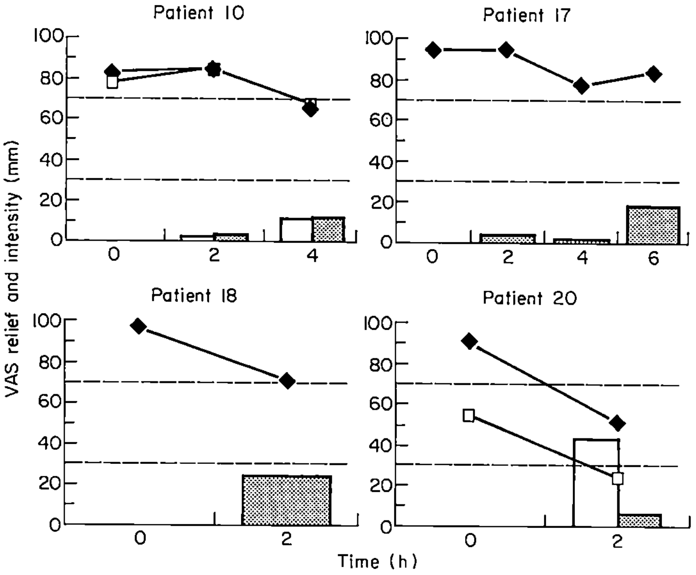

Fig. 2. Individual patients' analgesic response while taking PCA for those patients with 'poor' response (VAS pain relief score not > 30 mm at more than one assessment time). Patient 7 was unable to complete the VAS scales because of adverse events, and no figure for this patient is presented. Time (h) on the x-axis; VAS (mm) pain relief (columns) and pain intensity (lines) on the y-axes. Patients 10 and 20 had two pains.

able only with difficulty, and both patients had respiratory rates of 8 or 9 breath.min^{-1} at the same time as this drowsiness. In one of the patients (No. 7) this happened during the first 3 h on PCA after a total of 53.7 mg of morphine. In the other (No. 10) it occurred after 5 h on PCA, with a cumulative morphine dose of 133.9 mg. These two patients' determination to obtain pain relief was such that when woken for the assessments they pressed the button so many times that it was considered clinically unsafe to keep them on PCA.

Another patient in this group (No. 18) was withdrawn from PCA after 2.8 h because of severe drowsiness and a respiratory rate below 8 min^{-1} while sleeping. The remaining patient (No. 17) was withdrawn from PCA at 7 h. She demanded the maximum volume per hour during the whole period and, in spite of successive increases in the PCA morphine concentration (10 mg.ml^{-1} during first 2 h, 15 mg.ml^{-1} during the following 2 h and 30 mg.ml^{-1} during the last 2 h), she did not achieve more than 30 mm relief on the VAS. Although she had adverse events they were considered initially as acceptable. As further increases in dose were not possible (maximum available concentration of morphine for PCA was 30 mg.ml^{-1}), PCA was stopped and an intravenous infusion started. After 2 h on this infusion and a total morphine dose (PCA plus infusion) of 610.8 mg, the patient considered the adverse events to be unacceptable. She told the observer that they in fact had been unacceptable for the previous 6 h, but that she was trying to cope with them and obtain more pain relief. Pain relief, however, was never greater than 30 mm on the VAS.

Four patients (Nos. 3, 6, 12 and 16) had an analgesic response which was judged to be moderate. The basis of the 'moderate' judgement was the VAS pain relief score, which was more than 30 mm but less than 70 mm at two or more assessment times (Fig. 3). Patient 4 had pain at two sites, both judged clinically as neuropathic; for one of these pains he achieved a 'good' response, whilst the other was judged as a 'moderate' response.

The mean VAS pain relief and VAS pain intensity scores against time are shown for the groups of patients showing good, moderate and poor analgesic response in Figure 4. The other analgesic scales all showed similar change.

There were no significant differences in the baseline scores for mood or for the McGill pain questionnaire for the good, moderate and poor response categories (Table 2). Pains with good response had significantly ($p < 0.05$) lower mean baseline VAS pain intensity scores (72.1 ± 5.1 mm, $n = 14$, mean±sem) than those with moderate (87.9 ± 2.6 mm, $n = 7$) but not poor (85.4 ± 5.9 mm, $n = 7$) response. There was no significant difference in mood within response category between nociceptive and neuropathic pains at any time point.

Adverse events

In the group of pains judged to have a good analgesic response, two patients, (Nos. 2 and 5), never had adverse events, and nine patients (Nos. 1, 8, 9, 11, 13, 15, 19, 21, 22) had adverse events which were manageable (nausea and/or vomiting) or acceptable (drowsiness, headache, itching and/or lack of concentration). Two patients (Nos. 4 and 14) had either unacceptable and/or unmanageable adverse events. Patient 4 had persistent unacceptable nausea and vomiting in spite of three antiemetic interventions and also had unacceptable drowsiness. Patient 14 had severe unacceptable drowsiness after 8 h on PCA and withdrew from the study. This patient had moderate drowsiness before starting the study.

All the patients judged to have a moderate response on PCA, (Nos. 3, 6, 12 and 16), had unacceptable and/or unmanageable adverse events. Patient 3 had severe unacceptable giddiness and severe nausea and vomiting

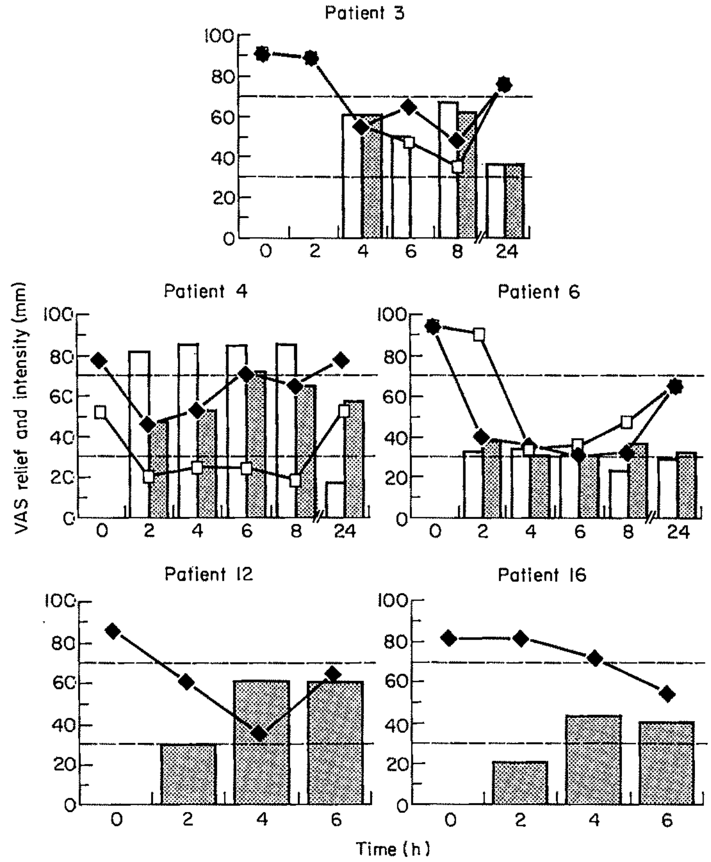

Fig. 3. Individual patients' analgesic response while taking PCA for those patients with 'moderate' response (VAS pain relief score more than 30 mm but less than 70 mm at 2 or more assessment times). Time (h) on the x-axis; VAS (mm) pain relief (columns) and pain intensity (lines) on the y-axes. Patients 4 and 6 had two pains.

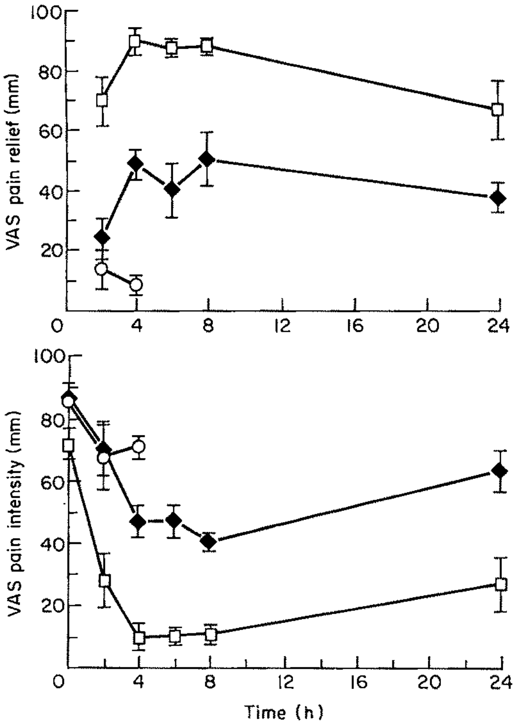

Fig. 4. Mean VAS pain relief and VAS pain intensity scores for PCA by response category. Mean (SEM), n = 14 pains for Good, n = 7 pains for Moderate and n = 7 pains for Poor. —— —— good, ——◆—— moderate, ——○—— poor.

which could not be controlled with four antiemetic doses. Patient 6 had no nausea but presented with simultaneous drowsiness, sweating, itching and lack of concentration, all rated as moderate; this combination was considered unacceptable by the patient. Patient 12 withdrew from the study after 6 h because of unacceptable nausea, dizziness, blurred vision, itching and dry mouth. Patient 16 was withdrawn after 6 h on PCA because of severe drowsiness and respiratory rate below 8 per minute while sleeping. The adverse events for patient 4 and for those with poor response (Nos. 7, 10, 17, 18, 20) were described above.

Morphine consumption and plasma concentrations

There were significant differences in PCA morphine consumption at the 2 and 4 h assessment times between the patients with poor response and those who had a moderate or good response on PCA (Fig. 5). No comparisons were made after the 4 h point because the poor response group was too small due to withdrawals from the study. There was no significant difference in the PCA morphine consumption between the patients with good and moderate response (Fig. 5) and nor was there any significant difference between the concentrations of either morphine or M3G for the different response categories, although plasma morphine and M3G concentrations were higher in the poor category than in good or moderate at all assessment times (Table 3). There were no significant differences at any

Table 3. Plasma concentrations (nmol.l^{-1}) of morphine and morphine-3-glucuronide what units? (M3G) while taking PCA. Values are expressed as mean (SEM), with the number of patients in the final parenthesis.

	Morphine			M3G		
Time; h	Good	Moderate	Poor	Good	Moderate	Poor
0	26.5 (19.6) (13)	4.8 (4.8) (5)	24.4 (17.7) (5)	607.1 (313.5) (13)	135.9 (122.2) (5)	679.6 (397.3) (5)
2	332.3 (55.3) (13)	439.6 (104.3) (5)	457.4 (62.3) (5)	2148.7 (398.8) (13)	2266.0 (531.3) (5)	3207.4 (559.4) (5)
4	280.9 (89.3) (13)	298.6 (44.9) (5)	479.3 (126.9) (3)	2773.9 (510.2) (13)	2185.8 (509.9) (5)	4292.7 (665.4) (3)
6	238.3 (91.3) (13)	168.1 (45.2) (5)	1535 (1)	2399.8 (501.2) (13)	2069.4 (502.8) (5)	10006 (1)
8	242.5 (90.8) (13)	131.9 (97.1) (3)	31692 (1)	2571.7 (637.9) (13)	2266.8 (1298.8) (3)	17762 (1)
24	128.9 (71.7) (10)	5.2 (3.9) (3)	ND	1019.2 (393.4) (10)	199.2 (65.1) (3)	ND

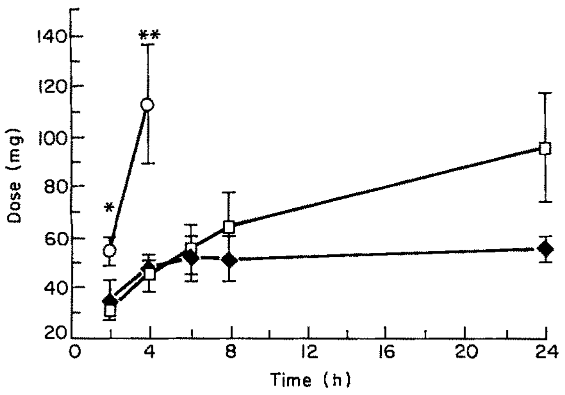

Fig. 5. Mean morphine consumption for PCA by response category. Mean (SEM), $n = 13$ patients for Good (12 at 24 h), $n = 5$ patients for Moderate (3 at 24 h) and $n = 5$ patients for Poor (3 at 4 h). Patient 4 had two pains, one good response and one moderate, and is therefore represented on both the good and moderate curves. ——□—— good, ——◆—— moderate, ——○—— poor. *significantly greater consumption in poor compared with good, ** = significantly greater consumption in poor compared with both good and moderate.

assessment time between the M3G:M ratios for patients in the three response categories.

Discussion

The results from this intensive descriptive study of a small number of patients fell into three categories. A substantial number of patients had an obvious response to morphine PCA. They titrated themselves to a position of adequate analgesia and were considered to have had a 'good' response. A small number had a negligible analgesic response, despite demanding significantly more morphine. They had unmanageable adverse events with little or no analgesia; they had a 'poor' response. Between these two categories a number of patients did not achieve the degree of analgesia seen in the good response category, despite similar morphine demand, and adverse events limited further increase in dose. These patients had a 'moderate' response.

'Good' responders showed VASPR of > 70 mm (Fig. 1) and 'moderate' responders > 30 but < 70 mm on at least two occasions during PCA (Fig. 3); 'poor' responders never had a VASPR > 30 mm on more than one occasion (Fig. 2). The arbitrary 30 and 70 mm levels used to make the distinction are justified by their adequacy in describing the data.

These different patterns of response were achieved despite significant difference in the amount of morphine demanded from the PCA system, the poor responders demanding significantly greater amounts of morphine at 2 and 4 h (Fig. 5), and indeed having significantly higher morphine plasma concentrations at these time points. There was, however, no significant difference (Table 3) between response categories for the M3G: morphine ratio (morphine-6-glucuronide analysis was not available), suggesting that there was no difference in morphine metabolism between the response categories to account for the difference in response.

An obvious problem with the method as described is the lack of placebo control. In theory these responses could be confounded by placebo response. Although a placebo effect is a plausible explanation of effective or augmented analgesia, it is less plausible as an explanation of no analgesia, and a number of patients in this study had poor analgesic efffect from morphine. The central observation of the study, the distinction between different response patterns to morphine, and particularly those patients with a poor response, is therefore unlikely to change even with placebo control. The method can be refined to alter the quantity of drug delivered per bolus, and then to judge whether or not the patient responds appropriately. The technical problems we have encountered with this approach include the timing of such an intervention. Made too early there is no constancy of demand history against which to measure the appropriateness of the response. Made late, as with control comparisons separated by weeks or even months, there is the problem of change in the underlying pain state. An alternative is to study the patient on more than one occasion using different concentrations of morphine.

The method, PCA with one trained nurse observer, worked well. The theoretical advantage in the chronic pain context of a method of testing opioid sensitivity without constraint as to dosage was borne out in practice. The constraint on dosage escalation came, as predicted [3], from adverse events. Again three categories were distinguished, in broad measure complementing the analgesic response categories. Among the good analgesic responders adverse events were a minor issue, absent or tolerable, with or without treatment. With the moderate analgesic responders, adverse events were more troublesome and resistant to treatment. In the poor analgesic response category, patients demanded significantly more morphine (Fig. 5) and adverse events were a major problem resulting in withdrawal from the study.

Scoring adverse event severity would have produced numbers to support this clinical judgement. We found ourselves hampered, however, in developing such a scoring system, because, while it was relatively easy to score adverse events which were tolerated with or without treatment, such as nausea or vomiting, the adverse events which resulted in withdrawal from the study were not so amenable to scoring. Some form of weighting is required if these response categories are to be explored further. Adverse event scoring should also take account of the increase in incidence if the patient is ambulant.

Although there was a convenient categorisation of adverse event incidence as the inverse of the analgesic response, the relationship between opioid dose, analgesia and adverse events may be complicated. The pain itself may act to counteract potential opioid receptor mediated adverse events from the opioid [11]. This mechanism might not operate for an opioid insensitive pain. Previous opioid exposure is also a factor; those with poor response and withdrawal from the study were more likely to have a higher ratio of morphine consumed on PCA to previous opioid dose (Table 2). This might be a circular argument, because the prescriber may have limited previous opioid dose suspecting or knowing that the response would be poor. The clinical suspicion remains that opioid adverse events are more problematic when the opioid dose is not 'balanced' by pain. On the evidence of this study the statement may be expanded to: opioid adverse events are more problematic when the opioid dose is not 'balanced' by an *opioid sensitive* pain. Until the mechanism of reduced

Table 4. Pre-study pain judgement and analgesic response category.

Prestudy judgement	Response Good	 Moderate	 Poor
Nociceptive	9	0	5
Neuropathic	5	6	2
Idiopathic	0	1	0

The numbers refer to individual pains (some patients had more than one pain).

sensitivity is understood, why this should be will remain unclear. Receptor systems other than opioid may well be operative, and some separation of effect and adverse event has been shown [12].

More troublesome than the *post-hoc* clarity of these response categories is the attempt to marry the response to either the prestudy clinical judgement of the pain, whether it was nociceptive, neuropathic or idiopathic, or indeed to the character of the pain (Table 2). The hypothesis was that nociceptive pain was opiate-sensitive, and that neuropathic pain was relatively insensitive. The prestudy judgement and the analgesics response outcome are shown in Table 4; there is no obvious difference between the distribution of cancer or of noncancer pains within the Table. Two cells in the Table are of particular interest; while five pains judged before the study to be nociceptive showed poor analgesic response, five pains judged before the study to be neuropathic showed good analgesic response. There are at least two explanations for these results, which conflict with the hypothesis. The first is that the hypothesis was wrong, that is that the *a priori* assumption of nociceptive pain equating with opioid sensitivity and neuropathic pain with insensitivity, is incorrect. The second is that the results are wrong. This could be the case if, for instance, a placebo effect was the explanation of good response in neuropathic pain, or if the prestudy clinical judgements of the pain were faulty. There was no evidence in this study of a differential opioid effect on mood between nociceptive and neuropathic pain, in contrast to a study which claimed an effect of morphine on pain 'affect' in neuropathic pain as opposed to an effect on pain 'sensation' [7].

The basis of the prestudy clinical judgement of neuropathic pain was that the pain was in an area with altered nervous system function. This judgement was predictive of moderate or poor response in just over half (8/13) of the pains judged to be neuropathic. The failure to predict the good response in 5/13 supports the opinion that adequate testing of opioid response in neuropathic pain is necessary before opioids are excluded from management [3], lest the proportion of pains which are capable of good or moderate response are denied opioid treatment when there is no other effective remedy.

One reason why the assumption of reduced opioid sensitivity in neuropathic pain is not the whole truth, is the multiple causes of neuropathic pain. To develop a definition of opioid insensitivity may require study of specific pain syndromes; even then, however, different mechanisms may apply [13]. The bigger surprise was the poor response of some of the pains judged to be nociceptive. Our assumption that nociceptive pain is always opioid sensitive is called into question. Chronic nociceptive pain may differ from acute nociceptive pain.

The expectation when using PCA opioid for pain relief is that patients will demand opioid in response to pain and will not demand opioid in the absence of pain. It is the pain or discomfort which is assumed to be the control variable in the feedback loop. Implicit in this expectation is the concept that the drug delivered will provide analgesia. The present study shows that when the drug delivered does not produce analgesia, and with a dogmatic instruction to continue demanding until complete pain relief is obtained, patients can achieve a potentially dangerous state because of the other central nervous system effects of the opioid. Our experience with this study suggests that the instructions which the patients are given may be critical in determining outcome. There is little placebo-controlled work with PCA, but failures of sensitivity in the acute pain setting [14] might be explained by failure of the instruction set to establish the same end-point. The response seen with PCA opioid in immunosuppressed patients with mucositis [15], where, by the criteria of this study, patients achieved only moderate and poor response, showed that within the same pain syndrome there was surprising inability to achieve a good (VASPR > 70 mm) response. Similarly, in postherpetic neuralgia, patients given morphine by infusion did not achieve a good response (mean data) by our criteria [8]. This supports the idea that different pains show different patterns of response to opioid; the extent to which these response categories are specific to a particular opioid, or may be generalised to all opioids, is unknown.

The clinical implications of this study centre on the answers to the three questions in the opening paragraph, which were: does reduced opioid sensitivity exist?, if so is it a relative rather than an absolute phenomenon? and are certain clinical pain syndromes predictive of different degrees of opioid sensitivity? We believe that the study distinguished different response categories to opioid, supporting the concept of reduced opioid sensitivity. In all but one patient (No. 7), some analgesic response was demonstrated; to that extent reduced opioid sensitivity is a relative rather than an absolute phenomenon. We studied a heterogeneous group of patients, so that judgement of prediction of different degrees of opioid sensitivity cannot be made. We did, however, attempt to correlate the response to our prestudy clinical judgement as to whether the pain was nociceptive or neuropathic. This correlation suggested that while the clinical judgement of neuropathic pain was a better predictor of moderate or poor response then chance alone, the reality is more grey than the black and white portrayal. The clinical difficulty then remains as to the prediction of these patients with poor or moderate response, in whom the dogma of persisting with dose escalation to achieve analgesia may be futile; failure to persist because of a neuropathic judgement would be a disservice to those whose pain could be well controlled. Such prediction may be possible using opioid challenge, as here with PCA, and for the majority of patients the response category was apparent in the first few hours. For the future, placebo or positive controlled confirmation of reduced opioid sensitivity would confirm these findings, follow-up would show the accuracy of the prediction of response and study within particularly pain syndromes might shed more light on both clinical prediction of reduced sensitivity and on mechanism. For the present, this study suggests that an operational definition of sensitivity can be made, and that this may be clinically useful.

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Isoflurane and propofol for long-term sedation in the intensive care unit

A crossover study

T. A. MILLANE, E. D. BENNETT AND R. M. GROUNDS

Summary

Propofol and isoflurane have been reported recently to offer better sedation than alternative agents in patients who require long-term ventilation in the Intensive Care Unit. This is the first report of a direct comparison between propofol and isoflurane. Twenty-four patients predicted to require artificial ventilation for at least 48 h were entered into a randomised crossover study to monitor sedation quality and time to recovery from sedation. There were no significant differences between the two agents in either end-point, with over 95% optimal sedation achieved by the use of each drug. Few adverse events were noted. Technological advances in the administration of volatile agents as long-term sedatives in the Intensive Care Unit may facilitate their more widespread use.

Key words

Intensive care.
Anaesthetics, intravenous; propofol.
Anaesthetics, volatile; isoflurane.

Most patients who receive artificial ventilation in the Intensive Care Unit (ICU) require sedation, particularly within the first 2 or 3 days, to enable them to tolerate both the tracheal tube and intermittent positive pressure ventilation. A number of intravenous agents have been used for this purpose. Recent interest has focused on propofol [1, 2] because this intravenous agent exhibits many of the features approaching those of the 'ideal' sedative [3]; any drug that is used for long-term sedation should be short-acting, noncumulative and free from adverse effects. In the past, Althesin and etomidate were used extensively, but their use in long-term sedation was discontinued because of serious adverse effects [4, 5]. Midazolam, a water-soluble benzodiazepine, has been used extensively; but there is evidence that it is not suitable for prolonged use in the critically ill [6, 7]. Although Bion and Ledingham reported in 1987 that 60% of ICUs in the UK used a combination of benzodiazepines and opioids for sedation [8], there is evidence that many units are now using propofol as the primary sedative agent [1, 9]. More recently, the volatile anaesthetic agent isoflurane has been used to provide short-term sedation for patients who require mechanical ventilation in the ICU; isoflurane has been shown to be superior to midazolam in this situation [10].

The purpose of this study was to compare, in a randomised crossover study, the efficacy of sedation with isoflurane and propofol, in the first 8 days on ICU in patients identified initially as requiring artificial ventilation for at least 48 h.

Methods

The study was approved by the local Ethics Committee and by the Committee of Safety of Medicines. Informed written consent was obtained from the patient, or when this was not possible from the next of kin. Consecutive male or female patients aged 18–80 years who were predicted to require mechanical ventilation of the lungs for longer than 48 h were entered into the trial. Exclusion criteria specified that the patient: should not be under an established regimen of sedation; should not require a neuromuscular blocking agent at entry to the study (except for the insertion of the tracheal tube); should not be grossly obese (> 150% of ideal body weight); should not have a head injury or be in coma; and should not be actively bleeding.

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A predicted requirement for opioid analgesia was not an exclusion criterion (unless a specific contraindication to the use of alfentanil existed).

Sedation regimen

The patients were stratified as 'medical' or 'surgical' admissions. An admission was considered 'surgical' only if the patient was admitted directly to ICU from the Operating Theatre. Once stratified, the patient was randomised to receive as a sedative agent either isoflurane (protocol A) or propofol (protocol B) for the first 24 h of admission, followed by the alternative drug for the second 24 h, and to continue the second drug up to and including 8 days from admission, or until sedation was no longer required, whichever was sooner. At the end of the first 24 h, the sedation regimen in use was stopped, and the time taken to the need for resedation was noted (washout period'. The second drug was continued until such time as sedative for a further 24 h; this consitituted the 'crossover period'. The second drug was continued until such time as sedation was no longer required, as described above.

The dose of sedative agent was adjusted to maintain a sedation level of 2–3 on the scoring system describd by Ramsay and his colleagues (Table 1) [11]. In the propofol group an intravenous infusion of 1% propofol (10 $mg.ml^{-1}$) was administered into a peripheral or central vein by an IVAC 711 infusion pump (IVAC, Basingstoke, UK). The infusion rate of propofol was recorded hourly and the nursing staff were allowed to adjust this as necessary, and to administer bolus doses of 20–50 mg as required. The total dose of propofol given was recorded to take account of such bolus doses. In the isoflurane group, a Mark 3 Isotec vaporizer (Ohmeda, UK) was attached to a Servo B ventilator (Siemens-Elema, Sweden) with a breathing system as shown in Figure 1; the vaporizer setting was adjusted to provide the required sedation level. The inspiratory concentration of isoflurane was measured continuously from the sample port in the patient breathing system as shown in Figure 1, using an infrared spectrometer (Datex, Helsinki, Finland); recordings were made hourly. Where rapid changes in the level of sedation were required, the inspiratory vaporizer concentration could be increased to produce a maximum inspiratory concentration of 2% for short periods (up to 2 min), at the discretion of the attending nurse. The total volume of liquid isoflurane used for each patient was recorded.

If necessary, a variable dose intravenous infusion of alfentanil (1 $mg.ml^{-1}$) was used concurrently to provide analgesia, and sedation was titrated in such a way as to allow the medical and nursing staff to obtain an indication of the requirement for pain relief from the patient. All other treatments (intravenous fluids, inotropic drugs, physiotherapy, neuromuscular blocking agents, etc.) were prescribed as deemed appropriate by the attending physicians in the usual way.

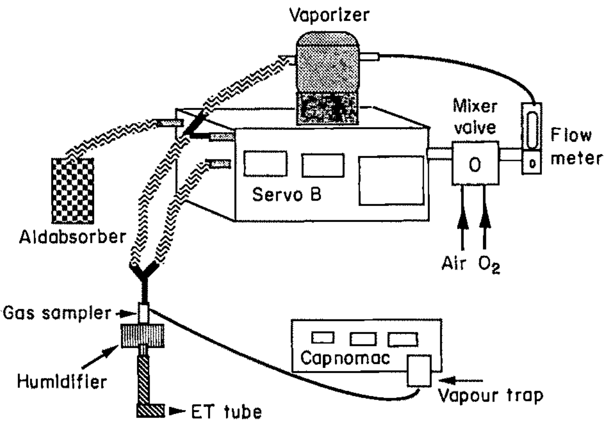

Fig. 1. Diagram of patient breathing system to show vaporizer in parallel.

Table 1. Ramsay scoring system for sedation [11].

Clinical score	Level of sedation
1	Anxious and agitated or restless
2	Co-operative, accepting of ventilation, oriented and tranquil
3	Asleep. Brisk response to light glabellar tap or loud auditory stimulus
4	Asleep. Sluggish response to light glabellar tap or loud auditory stimulus
5	No response to light glabellar tap or loud auditory stimulus, but responds to painful stimulus
6	No response to painful stimulus

Assessment of sedation

Sedation was monitored hourly by the nursing staff using the Ramsay scale as an objective assessment of sedation quality; additionally, the nurse was asked to record on a scale of 1–3 whether the level of sedation was thought subjectively to have been appropriate for that patient over the preceding hour (1 = poor; 2 = optimal; 3 = too deep).

At the end of each sedation period (washout period) the time taken for the patient to write his name and address was recorded. If the patient became unacceptably agitated before this, sedation was restarted, and the time and circumstances were noted.

Once it was deemed that sedation was no longer required, the time taken after discontinuation of sedation for the patient to write his name and address (response time), and time to extubation of the trachea, were recorded.

Cardiorespiratory monitoring

Heart rate and rhythm, arterial and central venous pressures, and core temperature were displayed continuously and recorded hourly throughout the period of the study. Cardiac output and pulmonary artery vascular parameters were measured and recorded if a pulmonary artery flotation catheter had been inserted for standard indications.

Respiratory rate, minute volume, peak airway pressure, inspired oxygen concentration and arterial blood gas measurements were recorded 6 hourly throughout the study, and every 15 min during the washout periods.

Laboratory assessments

The following laboratory assessments were made at study entry (baseline), at least daily throughout the study, and for 7 days after the completion of the study. *Haematology*: haemoglobin concentration, white cell count, packed cell volume, platelet count. *Biochemistry*: bilirubin, alkaline phosphatase, aspartate transaminase, alanine transaminase, gamma glutaryltransferase, total protein and albumin concentrations. *Renal function*: urine volume, and blood urea, serum creatinine and serum potassium concentrations. Serum inorganic fluoride concentration was measured in patients who received isoflurane for more than 24 h.

Statistical analysis

The paired or unpaired Student *t*-tests, Mann–Whitney *U*-test, and ANOVA (analysis of variance) were used as appropriate.

Results

Demography

Twenty-four patients were entered into the study. Demographic details, reasons for admission to ICU and the outcome for each patient are shown in Table 2. There were no significant differences between the treatment groups in terms of age, sex and illness severity. Thirteen patients were admitted to the medical group and 11 patients to the surgical group.

Medical group

Of the 13 medical patients entered into the study, six were randomised to protocol A (isoflurane for 24 h followed by propofol), and of these, all six received both agents, but only five completed the primary 48 h crossover period. The patient who did not complete the crossover could not be sedated successfully with either agent (patient 5). Four patients completed the study; sedation was administered successfully by isoflurane for 24 h, followed by propofol for 42, 43, 47, 48 h respectively, and all four were subsequently weaned from artificial ventilation. The fifth patient was sedated for 24 h with isoflurane and then for 28 h with propofol (patient 6). Although sedation with propofol was adequate, it was clinically obvious that better sedation had been achieved with isoflurane. Consequently, propofol was discontinued and isoflurane was restarted (as allowed for in the study protocol) and continued for a further 234 h.

The remaining seven patients were randomised to protocol B (propofol for 24 h followed by isoflurane). All seven received both agents; four completed the crossover period. Of the three who did not, one was weaned from ventilation at 38 h, and the other two died on the second day of the study. Of the four who completed crossover, one was weaned successfully at 72 h (48 h isoflurane), one died 80 h (56 h isoflurane) into the study and one was withdrawn from the study at 68 h (44 h of isoflurane) because of possible hallucinations (patient 11). The final patient was withdrawn at 107 h (83 h of isoflurane) due to equipment failure and subsequent inability to monitor inspiratory isoflurane concentration (patient 12).

Surgical group

Of the 11 surgical patients entered into the study, four were randomised to protocol A (isoflurane for 24 h followed by propofol). Of these, only one completed the crossover period and was weaned from ventilation at 50 h. Of the other three, two were weaned from sedation before crossover to propofol, and one returned to the operating theatre before crossover (patient 20).

The remaining seven patients were randomised to protocol B (propofol for 24 h followed by isoflurane). All seven completed the crossover period. Three were weaned successfully after 24, 48 and 151 h of sedation with isoflurane, one returned to the operating theatre after 48 h (patient 19), and the other three died after 24, 147 and 157 h respectively of isoflurane sedation.

Table 2. Demography and outcome.

Patient	Group	Age (years)	Sex	Reason for admission	Outcome
1	Medical	76	M	Pneumonia/portal vein thrombosis	Completed trial/hospital discharge
2	Medical	69	M	Pneumonia/COAD	Withdrawn day 2/ICU discharge
3	Medical	53	M	Lymphoma/Interleukin 2 toxicity	Died day 2
4	Medical	24	F	Heroin overdose/aspiration pneumonia	Completed trial/hospital discharge
5	Medical	68	F	Pneumonia	Withdrawn day 1/hospital discharge
6	Medical	43	M	Chickenpox pneumonitis	Withdrawn day 2/hospital discharge
7	Medical	69	M	Pneumonia, ARDS	Died day 2
8	Medical	76	F	Pneumonia/COAD	Completed trial/hospital discharge
9	Medical	80	M	Pneumonia	Completed trial/ICU discharge
10	Medical	67	M	Pneumonia/alcohol poisoning	Completed trial/ICU discharge
11	Medical	65	M	Pneumonia	Withdrawn day 3/died
12	Medical	51	M	Pneumonocystis pneumonia	Withdrawn day 5/died
13	Medical	69	F	Pneumonia/COAD/IHD	Withdrawn day 3/ICU discharge
14	Surgical	76	M	Elective aortic aneurysm repair	Withdrawn day 1/hospital discharge
15	Surgical	52	M	Hartmanns procedure/haemorrhage	Completed trial/hospital discharge
16	Surgical	56	F	Cardio-oesophagectomy/MOF	Completed trial/died
17	Surgical	64	F	Cardio-oesophagectomy/MOF	Completed crossover/died
18	Surgical	53	F	Cardio-oesophagectomy	Completed trial/hospital discharge
19	Surgical	46	M	Cardio-oesophagectomy/MOF	Completed crossover/died
20	Surgical	44	M	Cardio-oesophagectomy/volvulus	Withdrawn day 1/hospital discharge
21	Surgical	72	M	Jejunal bypass/ca oesophagus	Withdrawn day 1/hospital discharge
22	Surgical	64	M	Ruptured oesophagus/thoracic empyema	Completed crossover/died day 3
23	Surgical	37	F	Ischaemic colitis; DIC; ICH	Completed crossover/died
24	Surgical	73	M	Emergency aortic aneurysm repair	Completed trial/ICU discharge

COAD, chronic obstructive airways disease; IHD, ischaemic heart disease; ARDS, adult respiratory distress syndrome, MOF, multi-organ failure; DIC, disseminated intravascular coagulation; ICH, intracranial haemorrhage.

Table 3. Duration of sedation and recovery times.

Patient	Duration of sedation (h) Isoflurane	Duration of sedation (h) Propofol	Time to resedation (end day 1) min	Post-sedation response time (min)	Time to extubation (min)
1	24	42	120	300	360
2	14	24	60	15	Died
3	14	24	30	died	
4	24	48	13	15	1
5	0.1	0.1	Withdrawn		
6	24	28	5	Withdrawn	
7	14	24	15	Died	
8	24	24	15	5	Tracheostomy
9	24	48	2	15	25
10	24	42	10	1	60
11	44	24	25	Died	
12	83	22	1	Died	
13	56	24	5	2	Tracheostomy
14	18	0	30	Withdrawn	
15	151	24	30	30	Resedated
16	24	24	50	5	540
17	147	24	20	Died	
18	24	24	40	30	150
19	24	24	40	5	Died
20	21	0	5	Withdrawn	
21	6	0	5	Withdrawn	
22	24	24	5	Died	
23	157	24	60	Died	
24	48	24	55	10	110

Duration of sedation

Durations of sedation are shown in Table 3. Total duration of sedation with isoflurane (1013 h) was significantly longer than that with propofol (543 h) over the period of the trial, but median duration per patient was similar (median (range)) 24 (0.1–157) h for isoflurane, and 27 (0.1–48) h for propofol. The duration of sedation with each agent was not significantly different between medical and surgical patients, although the same pattern of longer sedation time with isoflurane was evident (median: medical v. surgical: isoflurane 24 v. 34 h; propofol 15 v. 24 h). A total of five patients (3 surgical, 2 medical) were sedated for a period in excess of 72 h; all five had been randomised to protocol B (propofol for 24 h followed by isoflurane for the remaining period). The three patients withdrawn on day 1 had all been allocated to protocol A.

Quality of sedation

Mean sedation scores for each agent are shown in Table 4 together with the respective nursing assessment of quality of sedation. Sedation scores during sedation with isoflurane were higher than during sedation with propofol, but on further analysis, this effect was confined largely to protocol A (Ramsay score isoflurane v. propofol: protocol A: 3.7 v. 3.0; $p = 0.02$, protocol B: 3.0 v. 2.8; $p = 0.98$). The nursing assessments of sedation quality did not differ significantly between groups (protocol A: 1.95 v. 1.91; $p = 0.83$, protocol B: 1.96 v. 1.94; $p = 0.98$). There were no differences in mean sedation scores or assessment of quality of sedation between the medical and surgical groups. Assuming an optimal sedation quality of 2.0, the sub-optimal sedation rates were similar for isoflurane and propofol (3.4% v. 3.6%).

Recovery from sedation

Recovery times for individual patients are shown in Table 3. The median (range) time to resedation after isoflurane sedation (protocol A) was 10 (2–120) min for the medical group and 18 (5–50) min for the surgical group. The median (range) time to resedation after the first 24 h of propofol sedation (protocol B) was 15 (1–16) min for the medical group and 40 (5–60) min for the surgical group. There was no significant difference between the agents (protocol A v. protocol B) in time to resedation after the first 24 h in the medical group or the surgical group. Taken as a whole, there was a trend toward a shorter time to resedation after isoflurane (median (range): protocol A v. protocol B: 10 (2–120) v. 28 (1–60) min; $p = 0.28$).

In patients who completed both days of the study and who subsequently fulfilled accepted criteria for weaning from ventilation, the median (range) time from cessation of sedation to being able to write their name was 10 (2–30) min in those who had received isoflurane ($n = 7$) and 15 (1–300) min for those who had received propofol ($n = 5$). This result is skewed by patient 1, and the differ-

Table 4. Quality of sedation.

	Isoflurane	Propofol	p value
Ramsay score mean (SD)	3.30 (0.79)	2.94 (0.68)	0.08
Sedation quality mean (SD)	1.94 (0.10)	1.93 (0.90)	ns
% sedation suboptimal*	3.4%	3.6%	ns

*see text.

ence is not significant. Time from stopping sedation to extubation of the trachea was 110 and 150 min in the two patients who had received isoflurane and 1, 25, 60, 360 and 540 min in the five who had received propofol; the small numbers preclude statistical assessment.

Sedation dose

The dose range of propofol was 0.4–9 (median 1.4) mg.kg^{-1}.h^{-1} (equivalent to 2–45 (median 9) ml.h^{-1}). The range of inspiratory concentration of isoflurane was 0.1–0.8% (median 0.35%). To take account of bolus doses of sedation, the total volume of each sedative per patient per day was calculated: propofol = 9–420 (median 40) mg.kg^{-1}.24 h^{-1} (48–2800 (median 240) ml.24 h^{-1}) and isoflurane = 76–600 (median 230) ml.24 h^{-1}. There was no significant difference in the doses of isoflurane or propofol administered on day 1 and day 2 of either treatment protocol. (Mean (SD) day 1 v. day 2 propofol: 11 (15) v. 6 (9) ml.kg^{-1}.day^{-1}; isoflurane: 369 (187) v. 357 (200) ml.day^{-1}). The dose of isoflurane administered depends upon both the concentration of isoflurane vapour and the minute ventilation. Since there were no significant differences in minute ventilation among the groups, the total volume of liquid isoflurane may be used as a comparitive measure.

Cardiorespiratory measurements

All patients were given inotropic and fluid support as indicated clinically, in order to maintain haemodynamic parameters within prescribed limits. As a result there were no significant differences between the groups for any cardiovascular parameter assessed (Fig. 2). Nine patients were monitored using a thermodilution pulmonary artery catheter. There were no significant episodes of hypotension attributable to the sedative agents in any of the patients, except in patient 5 (protocol A) who was withdrawn from the study because of significant reversible hypotension which occurred first with isoflurane and then with propofol. Sedation was achieved eventually with a combination of diamorphine and diazepam.

Laboratory tests

The assessment of haematological parameters revealed no unexpected abnormalities. Biochemical parameters were similarly unremarkable. Due to a technical error in the sampling technique, analysis of fluoride concentrations was possible in only eight patients, none of whom exhibited plasma fluoride concentrations in the toxic range.

Adverse effects of study medication

No adverse effects were attributable directly to isoflurane or propofol in cardiovascular (except patient 5, see above), respiratory, renal, haematological or hepatic systems. However, two patients who survived reported severe visual and auditory hallucinations during and after the study period. The same two patients developed a peripheral neuropathy (confirmed electromyographically) which resolved over the subsequent 4–12 months. Both patients had been randomised to protocol A and had received propofol for 24 h followed by isoflurane for 151 h and 254 h respectively. A third patient reported moderate visual hallucinations on the evening following the cessation of sedation, and on several subsequent days. This patient had also been randomised to protocol A and had received propofol for 24 h followed by isoflurane for 24 h. A fourth patient, randomised to protocol A, was withdrawn from the study after 24 h of propofol followed by 44 h of isoflurane sedation because it was suspected that hallucinations were occurring. This patient was sedated subsequently with midazolam, but confirmation of the hallucinations was not obtained due to death of the patient.

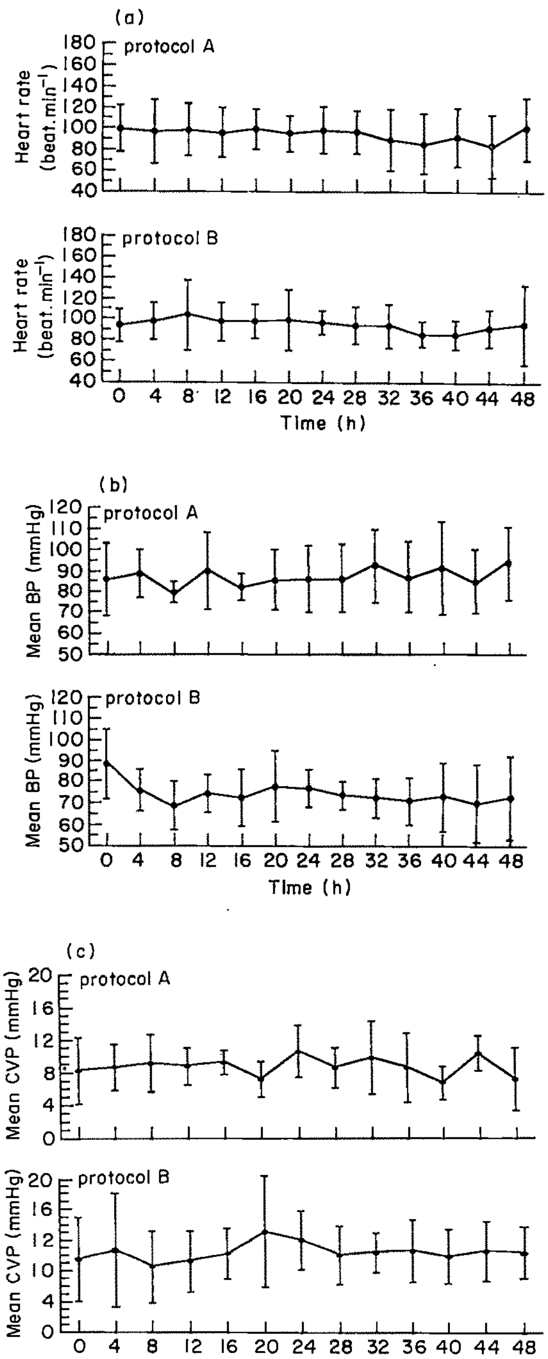

Fig. 2(a). Mean (SD) heart rate over first 48 h (crossover period). (b) Mean (SD) mean arterial pressure over first 48 h (crossover period). (c) Mean (SD) central venous pressure over first 48 h (crossover period).

Other drugs

Alfentanil was given to all patients in the surgical group and 8/13 in the medical group. There was a trend toward higher analgesic requirements in the surgical group; mean (SD) dose $\mu g.kg^{-1}.h^{-1}$: surgical 53.0 (42.3); medical 26.4 (16.7); $p = 0.11$. There was no difference in analgesic use between the two protocols (protocol A v. B:mean 44.8 v. 39.7 $\mu g.kg^{-1}.h^{-1}$). Six patients were given vecuronium during the course of the study period. These patients with severe respiratory failure required maximum ventilatory support, and muscle paralysis was considered appropriate clinically to allow adequate ventilation.

Discussion

There were no outstanding, statistically significant differences between isoflurane and propofol as assessed using the monitored variables. Both drugs appeared to be safe in 23 patients; in only one patient were adverse effects directly attributable to either drug seen. The results suggest that there is a trend toward a quicker recovery after long-term sedation with isoflurane compared to propofol, but the numbers are small, and further detailed analysis is not possible. The crossover design allowed a cautious interpretation of a comparison of sedation quality with the two agents within the same patient, and no significant differences were detected. However, objective sedation scoring indicated that sedation was deeper with isoflurane when this agent was administered on day 1, but that this effect did not extend beyond the first day. The subjective assessment of sedation quality offered by the nurses did not reflect the objective assessment, perhaps reflecting the different perceptions of the role of sedation held by nursing and medical staff. Whilst highlighting the need for objective assessment in such sedation studies, this observation is probably explained by the desire of the nurse to ensure adequate sedation on entry to the ICU whilst using a sedation agent with which he/she was less familiar. Despite the sedation assessment, the volume of sedative agent used did not differ between day 1 and day 2 for either drug.

Cardiovascular parameters were stable in all but one patient. This finding should be interpreted with caution, since both agents are known to cause hypotension in some circumstances. Our generally favourable experience with these drugs is probably explained by the Unit policy of aggressive fluid replacement, and early use of inotropic and/or vasopressor agents.

Other adverse features included the possibility that long-term use of isoflurane may cause hallucinations and/or a peripheral neuropathy; there are, however, no previous definite reports of either of these events in association with isoflurane, although worldwide experience with long-term sedation (more than 48 h) with this agent in man is limited to a few isolated case reports [12]. Speculatively, isoflurane may cause these adverse effects only in patients pretreated with propofol. As in Kong's study [13], fluoride accumulation was not seen, although, unfortunately, the data were incomplete.

Sedative agents administered by the intravenous route are used widely, and most intensive care staff are very familiar with their use. Problems with multiple infusions, poor venous access and incompatibility of solutions are well recognised, particularly when a bolus dose of sedative agent is required. The use of sedation administered by inhalation has its own inherent problems, not least of which, at least initially, is unfamiliarity with the agent and its route of administration. General points include the need for an appropriate vaporizer, a suitable ventilator and circuit, and an efficient scavenging unit [14].

This study had originally intended to use the Siemens-Elema vaporizer which fits directly on to a specially adapted Servo B ventilator, between the air–oxygen mixer valve and the ventilator gas inlet port. In theory, this calibrated vaporizer should deliver a known concentration of volatile agent to the patient, obviating the need for complex and expensive equipment for continuous measurement of inspiratory concentration of the drug. However, we noted that the quantities of liquid isoflurane used bore little resemblance to the vaporizer settings. Using a Capnomac to measure inspiratory isoflurane concentrations, we demonstrated a considerable variation in delivered concentrations as the volume of isoflurane within the vaporizer decreased. Consistent demonstration of this characteristic, using a variety of vaporizers and ventilators, led to the withdrawal of these vaporizers from use in our institution.

An alternative system, using an Isotec vaporizer, was eventually devised. The resultant circuit is particularly clumsy (Fig. 1), and a Capnomac is required to monitor the inspired concentration. Furthermore, it has been suggested that end-tidal partial pressure of isoflurane is a poor predictor of its arterial partial pressure [15]. However, as a direct result of our experiences, a Penlon OMV drawover vaporizer has now been developed, which is placed distal to the ventilator in the patient breathing circuit. This vaporizer is compatible with all ventilators, and delivery is accurate to 0.1%, thus obviating the need for complex circuitry and continuous Capnomac recording of inspired isoflurane concentration.

Many actions involved with the general care of the patient on ICU involve temporary interruption of the ventilator circuit; thus, unlike intravenous agents, a continuous supply of a volatile agent is not always ensured. Tracheal suction, physiotherapy and the administration of nebulised drugs are performed frequently. Special problems arising with isoflurane were caused by its short duration of action. Within a few minutes of 'Ambubag physiotherapy', sedation was inadequate, and frequent 'top-ups' with isoflurane were required, necessitating reconnection to the ventilator circuit. Intermittent high dose delivery of sedative agents increases the risk of adverse reactions, particularly hypotension, and thus are far from ideal. Further modifications to the ventilator circuit are planned, but at present these practical issues do represent a drawback to more generalised use.

There are few studies of long-term sedation in the critically ill, and none involving both propofol and isoflurane. Direct studies of isoflurane and propofol, used with or without nitrous oxide, have been limited to the peri-operative period [16, 17, 18]; in all these studies of patients undergoing day case surgery, recovery was quicker after anaesthesia with propofol than with isoflurane. Similar findings were reported by Doze *et al.* [19] for short-term anaesthesia, but interestingly, no difference in recovery time or incidence of postoperative side effects was noted in longer term anaesthesia with propofol compared with isoflurane during major operative procedures [19]. Our findings are in keeping with this observation. There are few studies of sedation in ICU. Kong [10] reported an open comparison of midazolam and isoflurane for sedation for up to 24 h in the ICU and concluded that recovery from isoflurane was significantly quicker than with midazolam; in addition, quality of sedation was better in the isoflurane group. Aitkenhead [20] reported faster recovery from sedation after propofol compared to midazolam, whilst Harris [2] reported little difference in sedation quality between propofol and papaveretum/midazolam (this study did not report recovery times).

We recognise that our study has some limitations. Only seven of the 24 patients (17%), with a wide range of pathology, completed the study; nine patients died and eight were withdrawn. Studies in ICU are hampered by heterogeneity and high mortality, a point particularly relevant to a study which stipulated as an entry criterion that patients should be predicted to require artificial ventilation for at least 48 h. The study design attempted to avoid some of the bias arising from heterogeneity by randomising patients in two groups (medical and surgical) in a crossover fashion, and direct comparative analysis was limited to patients who completed the entire 48 h primary study period.

In conclusion, no significant differences were detected between isoflurane and propofol in terms of sedation quality or time to recovery from sedation. Both agents appear to be safe, and few adverse events directly applicable to either agent occurred. Practical problems with the administration of isoflurane have been largely overcome, and further technological modification is planned.

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The Riyadh Intensive Care Program applied to a mortality analysis of a teaching hospital intensive care unit

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Summary

A computerised system of prediction of death using the Riyadh Intensive Care Program was applied retrospectively over a 17-month period to data collected prospectively on 1155 patients admitted to our intensive care unit. Variables which enable organ failure scores to be generated were recorded daily to make these predictions. Consultant medical opinion predicted that outcome was hopeless in 55% (115/209) of the patients who died. The predictive power of the computer demonstrated a sensitivity of 14.8% and a specificity of 99.8%. It is possible that the occurrence of three false predictions of death in the latter part of the series may have been related to a change in our antibiotic policy. We would be unhappy to recommend the general use of a computerised program for prediction of death without careful explanation of its significance and dangers.

Key words

Intensive care;
Complications; death.

Outcome of patients in the intensive care unit (ICU) reflects factors which may be patient-dependent or treatment-dependent. The most important patient factors are the severity of illness, the nature of the disease process causing the critical illness and the response to treatment. Frequently, it is difficult to make an exact diagnosis in many critically ill patients on initial referral for admission to ICU and a patient's response to treatment can never be anticipated with any certainty among the broad case mix seen in a general ICU. This is the reason that it is difficult to undertake triage of patients for admission to ICU. It is generally accepted that if any patient has a chance of survival when first referred for ICU admission, and if there is an ICU bed available, then that patient should be admitted. One retrospective analysis of the utilisation of an ICU [1] showed that among a group of 480 general ICU patients it was possible to identify 86 (18%) who would never, or would no longer, have benefited from ICU admission using five criteria (perceived need for ICU care, response to therapy, individual prediction of death, hospital outcome and basic clinical data). This group of patients was shown to use 27% of the total bed occupancy. It is well recognised that there is an inverse relationship between outcome and costs in ICU [2]. However, because of the problems of triage on admission, it is inevitable that a number of patients will be admitted to ICU with a hopeless prognosis. Treatment of the critically ill with a hopeless prognosis is wasteful of precious medical resources, as well as having a demoralising effect on the nursing staff and the patients' relatives. Thus for the efficient running of an ICU and for humanitarian reasons it is important to take a decision to withdraw treatment on all patients whose outcome is considered to have become hopeless.

Normally, a decision to withdraw therapeutic support from a critically ill patient is taken following discussion between the ICU consultant, the referring specialist and relatives. The decision is invariably taken with compassion and with due regard to the known wishes of the patient and his family. The problem for the ICU doctors and involved specialists rests on the proper identification of patients with a hopeless prognosis. The Riyadh Intensive Care Progam [3–5] has been shown in one institution to be reliable in predicting outcome in the critically ill. This program uses trend analysis of daily APACHE II scores [6] corrected for the number and duration of organ failures to derive Organ Failure Scores (OFS) [4]. The APACHE II score is based on the deviation from normal of 11 acute physiological variables (rectal temperature, mean blood pressure, heart rate, respiratory rate, oxygenation, arterial

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pH, serum sodium, potassium, creatinine, haematocrit and white cell count) and the Glasgow Coma Score (GCS), the patient's age, and the presence of defined chronic disease. Criteria adapted from Knaus [7] and Garden [8] were used to define major organ system failure. This required the use of additional variables (occurrence of ventricular fibrillation or tachycardia, number of days dependent on a ventilator, urine output, serum urea, platelet count, prothrombin ratio and the presence of hepatic encephalopathy).

No reports of a false prediction of death have so far been reported with the Riyadh Intensive Care Program, and so we were interested to determine if it could help with clinical decision making in our ICU.

Patients and methods

The University Hospital of Wales is a 799-bedded teaching hospital. It is a referral centre for the whole of South, Mid and West Wales and is the only hospital in the region to specialise in cardiac surgery. There is also a specialist Neurosurgical Unit, but no orthopaedic facility. Multiple trauma patients admitted because of severe neurosurgical or chest trauma are potentially compromised because of a lack of resident orthopaedic cover and operating facility. Patients who require orthopaedic operative treatment must be transferred to another hospital in the city and if they have concomitant neurosurgical injury, they must be returned the same day. There is no renal dialysis unit in our hospital and patients who require renal support are treated with peritoneal dialysis if considered suitable. Patients who require haemofiltration or haemodialysis are transferred to another hospital in the city. Funding for the capital and revenue haemofiltration costs have never been available for our ICU.

Our ICU can be classified according to the administrative classification defined by the National Institute of Health (NIH) Consensus Conference on Critical Care [9] as Level 1. It is a 10-bedded ICU with a mix of adult cardiac, neurosurgical and general surgical patients in addition to adult medical and paediatric cases. There is one full-time and two part-time consultant intensivists. The junior doctors are registrars from the department of anaesthesia; they remain on the ICU continuously for 24 h periods. The ratio of nursing staff to patients is always 1 : 1 and there is always an experienced nursing sister in charge on each shift.

All adult patients admitted to our ICU from May 1989 to October 1990 were assessed daily by the APACHE II, APACHE II Risk of Death and OFS. Six hours was the minimum period used in the collection of data for a day 1 assessment. Data from shorter periods were carried over to the following day, which was then regarded as day 1. We did not collect data on the day of death or discharge except for those patients who died or were discharged on day 1 and had been in the ICU for at least 6 h. The worst values for the acute physiological variables and the best GCS were collected for each day to generate APACHE II scores. One thousand one hundred and ninety-eight consecutive admissions to our ICU from May 1989 to October 1990 underwent daily OFS assessment. Full hospital outcome details were availabe for 1155 (96%) of the original 1198 patients at the time of this analysis. The basic characteristics of these 1155 patients are shown in Table 1.

Table 1. General information from 1155 ICU patients.

	n	%
Males	766	66.3
Mean age 58 years		
Females	389	33.6
Mean age 59 years		
Major systems affected		
Respiratory	130	11.2
Cardiovascular	866	74.9
Gastrointestinal	13	1.1
Neurological	131	11.3
Metabolic	5	0.4
Haematological	7	0.6
Renal	3	0.2
Positive for chronic ill health		
Liver	3	0.2
Cardiovascular	728	63.0
Pulmonary	27	2.3
Renal	6	0.5
Depressed immunity	54	4.6
Significant categories		
Nonoperative	208	18.0
Postoperative	947	81.0
Emergency surgery	155	13.4
Elective surgery	792	68.5
Operative complications	15	1.3
Transfers from other wards	113	9.7
(mean days before transfer 6)		
Transfers from other hospitals	45	3.9
(Mean days before transfer 5)		
Emergency room admissions	50	4.3
Outcome analysis		
Died in ICU	136	11.7
Mean length of stay	7 days	
Discharged alive	1019	
Mean length of stay	3 days	
Died in hospital	209	18.1
Mean length of stay	9 days	
Discharged alive	946	
Mean length of stay	12 days	

It is our policy to discharge patients from the ICU only when satisfactory spontaneous ventilation can be maintained either via the patient's natural airway or via a tracheostomy, and when haemodynamic stability has been achieved. Treatment is withdrawn from patients only if the consultant intensivist and referring specialist agree that the patient's outcome is hopeless. The relatives are notified of the decision and the situation is fully explained to them. The withdrawal of treatment involves cessation of inotropic infusions or reduction in the delivered oxygen concentration towards normal. Artificial ventilation is never terminated in patients who are dependent on it. Terminally ill patients are always well sedated. All patients predicted to die by the clinicians, and in whom treatment is withdrawn, invariably die within 12 h of cessation of treatment, and usually within 1 h if dependent on inotropic support.

Computerised trend analysis of daily OFS was used to predict hospital outcome of each patient studied, but the data for predicting outcome were never entered into the computer until after the patient had left ICU. Thus, these formal predictions were never known to the treating physician in real time, and thus could never have been used to influence clinical decision-making. The mortality ratio was calculated by dividing the actual mortality by the expected mortality, derived from the mean APACHE II Risks of Death on day 1.

We used ICU bed days as a measure of the utilisation of ICU resources. During the study period there were a total of 4980 adult ICU bed days available. The 1198 adult patients treated used 4138 bed days, a bed occupancy rate of 83%. The 1155 patients analysed in this study occupied 4009 bed days. We noted the number of ward days after discharge, but not those before admission.

One of us collected data prospectively on special forms every day and followed the hospital outcome of patients discharged alive from ICU. The Riyadh Intensive Care Program was written in dBase III plus (Ashton Tate) to generate OFS, APACHE II score, Risk of Death and outcome predictions on an IBM AT compatible computer. We used Statgraphics (Statistical Graphics Corporation) for statistical evaluation on the microcomputer. Where appropriate, the Student *t*-test and Fisher's Exact test were employed.

Analysis of predictive power

We classified the prognosis of patients as either 'unknown' or 'predicted to die', rather than the usual 'predicted to live' and 'predicted to die' to reflect more closely what happens in practice. In clinical settings, the outcome of patients is regarded as unknown and they are treated with the aim of achieving survival until a decision is made to withdraw treatment from those whose prognosis is considered to be hopeless. The following terms were used to express the predictive power: specificity (unknown predictions surviving/total survivors); sensitivity (true prediction of death/total deaths); false-positive diagnosis rate (false prediction of death/total predictions of death); false-positive rate (false prediction of death/total patients).

Results

The total adult mortality (Table 1) in this study was 18% (209/1155). Patients who had undergone cardiac surgery comprised 67% (770/1155) of our total admissions, and mortality in these patients was 4.5% (35/770). Thus, mortality in other adult patients was 45% (174/385). Chronic ill health was present in 70% (818/1155) of our patients. Mortality among the various chronic ill health groups is shown in Table 2. Twelve percent (96/818) of the patients with chronic ill health died. Chronic ill health was present in 46% (96/209) of nonsurvivors. The mean (SD) day 1 OFS of survivors was 13.5 (4.7) and compared with 19.9 (7.0) for nonsurvivors ($p < 0.001$). The mortality in the various OFS bands are shown in Table 3. The mortality ratio was 1.27.

Table 2. Mortality rates in patients with chronic ill health.

	n	Nonsurvivors (%)
Cardiovascular	728	55 (8)
Immunological	54	28 (52)
Respiratory	27	10 (37)
Renal	6	2 (33)
Liver	3	1 (33)
Any chronic ill health problems	818	96 (12)
No chronic ill health problems	337	113 (34)

Table 3. Mortality rates associated with different bands of organ failure score.

Band	*n*	Nonsurvivors (%)
0–9	273	21 (7)
10–19	716	90 (13)
20–29	149	82 (56)
30–39	16	15 (94)
> 39	1	1 (100)
Total	1155	209 (18)

Using the data which were collected prospectively, the nonsurvivors were grouped retrospectively into three groups: those for whom the earliest prediction of death would have been made by the computer, those for whom it was first made by the ICU consultants, and those in whom treatment was not withdrawn (Table 4). The computer predicted death in 34 patients. In this group there were three patients who were falsely predicted to die by the computer but not by the treating consultants. In order to assess the statistical significance of this finding, we have identified 116 cardiac surgical patients over a 3.5 year period (unpublished data) who were predicted to die; all died. Over the last 4-month period of this study, nine cardiac surgical patients were predicted to die by the computer, but three survived. This is a statistically significant difference ($p < 0.005$, Fisher's exact test). The predictive power of the computer is shown in Table 5. The 31 patients who were correctly predicted to die were eventually considered to have a hopeless prognosis by the consultants responsible for them, and treatment was withdrawn. The diagnostic groupings and basic data of this group are shown in Table 6. The five patients grouped as 'brain-stem dead' were predicted to die by the computer before they had fulfilled the criteria for brainstem death. This group of patients was excluded from the brainstem dead patients shown in Table 4.

Patients with cardiogenic shock or septic shock were predominantly elderly and had mean (SD) ages of 64.7 (14.4) and 66.3 (9.9) years respectively. Criteria for defining acute oliguric renal failure were: urine output $<$ 479 ml.24 h^{-1} and serum urea > 35.7 mmol.l^{-1} or serum creatinine > 308 μmol.l^{-1}. Acute oliguric failure occurred in 45% (14/31) of these patients. The mean (SD) serum creatinine concentration in the 31 patients was 400.0 μmol.l^{-1} (208.1); 97% (30/31) had developed acute tubular necrosis. The mean Risk of Death of these patients, excluding the brainstem death patients, was 39.1 (SD 25.0, SEM 5.1).

Table 4. Prediction analysis using the Riyadh Intensive Care Program in 209 deaths which occurred among 1155 consecutive admissions to ICU.

Outcome prediction group		*n*	(%)
Predicted to die initially by the computer		31	15
Predicted to die first by ICU doctors		84	40
Brainstem dead	27		
Not brainstem dead	57		
Not predicted to die		94	45
Total		209	100

Table 5. Predictive power of the computer among 1155 consecutive admissions to ICU.

	Actual dead	Actual alive	Total
Predicted to die	31	3	34
Outcome unknown	178	943	1121
Total	209	946	1155
Sensitivity (%)		14.8	
Specificity (%)		99.6	
False positive diagnosis rate (%)		8.8	
False positive rate (%)		0.2	

Two of the three patients, whose death was predicted incorrectly by the computer, underwent triple coronary artery bypass grafting and developed bronchopneumonia and septic shock syndrome (in one case, *Enterobacter cloacae* was grown from the blood). Both of these patients developed failure of two organ systems in addition to severe renal dysfunction (maximum serum creatinine concentrations of 233 and 279 μmol.l^{-1}) due to acute tubular necrosis. They were both predicted to die on ICU day 5, with OFS of 29.5 and 29.6. The third patient underwent repair of a ventricular septal defect secondary to myocardial infarction. He was in cardiogenic shock on return to ICU from the operating theatre, with a cardiac index of 1.5 l.min^{-1}.m^{-2} and a pulmonary artery wedge pressure of 25 mmHg. This patient had failure of three organ systems including oliguric renal failure (maximum serum creatinine concentration 418 μmol.l^{-1}) and required renal support (peritoneal dialysis) for 5 days. He was predicted to die on the second ICU day with an OFS of 31. All three patients were assigned a prediction of death on one occasion only. All patients were treated with a non-nephrotoxic antibiotic. They were discharged home well and continue to remain so. They all enjoy an independent existence up to 12 months following hospital discharge.

If a decision to withhold treatment had been taken at the same time as the computer prediction (provided death had supervened within 24 h) the total number of potential ICU and ward days saved would have been 132 and 8 days respectively. This would have presented a saving of only 2.8% of total ICU adult bed days.

Table 6. Principal diagnostic groupings of 31 patients in whom the computer predicted death.

Diagnostic group		*n* (%)	Mean (SD) age; years
Brainstem dead		5 (16)	49.2 (19.2)
Trauma	2		
Post-op AA repair	1		
Post-op CABG +MVR	2		
Head injury (GCS < 8)		2 (7)	31.5 (14.8)
Septic shock (abdominal)		6 (19)	66.3 (9.9)
Cardiogenic shock		14 (45)	64.7 (14.4)
Post-op AA repair	2		
Post-op MVR	3		
Post-op CABG	3		
Cardiac arrest	4		
MI	2		
Neoplasm		4 (13)	42 (24.5)
Myeloid leukaemia	3		
Hodgkins	1		
Total		31 (100)	50.7 (16.6)

AA, aortic aneurysm; CABG, coronary artery bypass graft; MVR, mitral valve replacement; GCS, Glasgow coma score; MI, myocardial infarction.

The consultants considered 55% (115/209) of the nonsurvivors to have a hopeless prognosis and withdrew therapy. These 115 patients comprised 84 patients who were considered to have a hopeless prognosis by the ICU doctors only and 31 patients who were predicted to die initially by the computer, and subsequently by the consultant medical attendants. Of these 84 patients, 27 (33%) were diagnosed as fulfilling all the criteria and brainstem death [10]. Brainstem death was due to haemorrhage into a brain tumour in one patient, subarachnoid haemorrhage in 12, severe trauma in nine, and cerebral anoxia in five. Of the 57 patients predicted to die from causes other than brainstem death, 28% (16/57) fulfilled Knaus' criteria for acute oliguric renal failure. The mean (SD) serum creatinine concentration of these 57 patients was 265 (186) μmol.l^{-1}; 72% (42/57) had suffered acute tubular necrosis.

The principal diagnosis and basic data of the 57 patients in whom treatment was withdrawn (excluding the brainstem dead patients) are shown in Table 7. The mean Risk of Death in this group (excluding seven neurosurgical patients) was 34.9 (SD 18.5, SEM 2.6). The four patients with chronic obstructive airways disease suffered either from end-stage disease, or from other major system disease; two had undergone oesophagectomy for neoplasm of the oesophagus, one suffered from polyarteritis nodosa and was on a high-dose steroid regimen, and one developed pulmonary aspergillosis following a bout of influenza (the last patient developed acute oliguric renal failure).

There were 94 nonsurvivors in whom treatment was not withdrawn; 28% (27/94) of these patients died within 72 h of admission and 70% (65/94) died on the wards and not in ICU. The principal diagnosis and basic data of this group of patients are shown in Table 8. The mean Risk of Death of this group (excluding 20 neurosurgical patients) was 28.3

Table 7. Principal diagnostic groupings among 57 patients in whom treatment was withdrawn.

Diagnostic group		*n* (%)	Mean (SD) age; years
Neurological (GCS < 8)		7 (12)	49.3 (20.7)
Head injury	1		
ICH	6		
Septic shock (abdominal)		14 (24)	70.0 (9.2)
Acute liver failure		3 (5)	47.0 (25.1)
Cardiogenic shock		18 (31)	66.7 (5.6)
Cardiac arrest	2		
Post-op MVR	4		
Post-op CABG	1		
Post-op AA repair	5		
Pulmonary embolism	2		
CCF	3		
MI	1		
Neoplasm		11 (19)	55.0 (22.3)
Myeloid leukaemia	6		
Oesophageal Ca	5		
COAD		4 (7)	65.4 (9.8)
Total		57 (100)	58.9 (15.5)

GCS, Glasgow coma score, ICH, intracranial haemorrhage; MVR, mitral valve replacement; CABG, coronary artery bypass graft; AA, aortic aneurysm; CCF, congestive cardiac failure; MI, myocardial infarction; Ca, carcinoma; COAD, chronic obstructive airways disease.

Table 8. Principal diagnostic grouping of 94 survivors who were not predicted to die.

Diagnostic group		*n* (%)	Mean (SD) age; years
Neurosurgical		20 (21)	53.5 (15.0)
Head injury	7		
SAH	11		
Neoplasm	2		
Sepsis/septic shock		18 (19)	61.0 (15.0)
Low cardiac output states		39 (42)	65.9 (12.6)
Post cardiac surgery	18		
Post MI	5		
CCF	4		
Aortic aneurysm	8		
Post cardiac arrest	1		
Hypovolaemic shock	3		
Neoplasm		12 (13)	61.5 (13.2)
COAD		3 (3)	68.3 (11.7)
Miscellaneous		2 (2)	64.3 (8.9)
Total of all patients		94 (100)	64.4 (12.7)

SAH, subarachnoid haemorrhage; MI, myocardial infarction; CCF, congestive cardiac failure; COAD, chronic obstructive airways disease.

(SD 20.9, SEM 2.5). None of these patients satisfied the criteria for acute oliguric renal failure.

Discussion

Clinicians are usually reluctant to exclude any critically ill patient among the broad case mix referred for admission to a general ICU because of the problems of triage and our inability to predict a patient's response to treatment. A decision to withdraw treatment backed by an accurate prediction of death after a trial period of treatment is more readily acceptable to clinicians, patients and their relatives. The Riyadh Intensive Care Program has been shown in a report from a single institution to be a more reliable predictor of outcome than either experienced clinicians or intensive care nurses [5].

We have shown in this study that predictions in the Riyadh Intensive Care Program's outcome were not as impressive as those demonstrated previously in a very different medical population. The sensitivity of prediction of death (proportion of deaths predicted) was only 14.8% in this study. The bed days which would have been saved, expressed as a percentage of the proportion of total ICU bed days occupied by nonsurvivors, was only 2.8%; in a previous study it was considerably higher (27%) [1]. Three patients were falsely predicted to die by the computer (but clearly not by the treating physicians); all three false predictions occurred in the last 4 months of this study. This was significantly different to the findings in an earlier period in which no false positive predictions occurred ($p < 0.0005$), and we believe that it may be related to a change in our antibiotic policy. Previously, a policy had been adopted of using gentamicin, cefuroxime, and metronidozole for life-threatening infections such as septic shock states and aspiration pneumonia. The rationale for using antibiotics prophylactically in low-output states is that splanchnic ischaemia due to poor general perfusion may lead to invasion by gut organisms and absorption of endotoxins from the gut wall; this has been postulated as a cause of irreversible shock [11,12]. It has been shown that prophylactic antibiotics improve survival in animals with gut ischaemia [13]. Our new policy, in consultation with the Department of Microbiology, is to administer a non-nephrotoxic broad spectrum antibiotic with good tissue penetration in these situations. It has already been suggested that a prediction of death might be a novel way of testing the efficacy of new therapeutic modalities [5]. The possibility that our change in antibiotic policy could have been an important factor in determining survival in three patients falsely predicted to die by the computer deserves further careful consideration and investigation.

Our mortality ratio was high (1.27) but no allowance was made for selection and lead-time bias [14]. For example, there was a 44% mortality rate among 11% (131/1155) of our patients who had neurological problems. The mortality ratio of the remainder of the patients (i.e. excluding those with neurological problems) was 1.01. This can be explained by our policy of giving patients the best or normal GCS in cases where it is difficult to ascertain the score. This policy tends to underestimate the APACHE II score and Risk of Death, and thus to increase the mortality ratio. There was a high incidence of chronic disease (46%) among the nonsurvivors and some of these patients may have been in end-stage organ failure when admitted to the ICU.

Presentation of the data on outcome prediction using the Riyadh Intensive Care Program has never been intended to promote general use of the program in its present form. We consider that the data on outcome predictions with the Riyadh Intensive Care Program have always been presented in a responsible manner. However, we advocate extreme caution in the use of any computer system which predicts death, and advise a careful explanation of its functioning and dangers.

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CASE REPORT

Acute isoniazid poisoning

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Summary

We present two cases of acute isoniazid poisoning in patients who ingested 7.5 g and 5.0 g of isoniazid respectively, with the intention of committing suicide. Both were admitted unconscious, with ventilatory insufficiency and convulsions. Hepatic dysfunction and peripheral neuropathy were notable complications.

Key words

Toxicity; isoniazid.
Complications; convulsions, hepatic, neurological.

Tuberculosis is a major public health problem, especially in Third World countries; even in some developed countries its incidence is 2–3% in the age group 0–14 years. In India the prevalence of natural infection is about 40% in all age groups [1]. Isoniazid (INH) is a first line drug in the treatment of tuberculosis. Chronic isoniazid toxicity has been reported in patients taking this drug for therapeutic purposes [2]. However, acute isoniazid poisoning as a result of attempted suicide is extremely rare. The acute ingestion of large quantities of isoniazid is known to cause severe toxicity and death as a result of recurrent seizures [3]. We report the successful treatment of acute isoniazid poisoning in two patients.

Case histories

Case 1

A 23-year-old woman was admitted in coma to the critical care unit about 5 h after consuming 75 tablets (7.5 g) of isoniazid having started convulsing at home. A rapid examination showed a tachypnoeic patient (respiratory rate 32 breath.min^{-1}) with sluggish protective airway reflexes but no other abnormal clinical signs. After oxygenation, tracheal intubation was performed with a cuffed tube and intermittent positive pressure ventilation (IPPV) was started, with an $F\text{IO}_2$ of 1.0. Once the airway was secured, gastric lavage was performed with 2 l of physiological saline. A detailed history obtained from relatives revealed that the patient, who was 6 weeks pregnant, had consumed INH with suicidal intent. The fact that her mother was being treated for pulmonary tuberculosis, gave her ready access to the drug. She had a further episode of generalised convulsions for which diazepam 5 mg was given intravenously. The convulsions stopped for a few minutes, only to recur. Diazepam 5 mg was repeated and phenytoin 300 mg was given as an intravenous bolus dose, followed by 75 mg 8 hourly. At the same time an infusion of pyridoxine 7.5 g in dextrose 5% was started. The convulsions were still not controlled, therefore a bolus dose of thiopentone was given, followed by an infusion of thiopentone 0.1% at a rate of 100 mg.h^{-1} (2 mg.kg^{-1}.h^{-1}). Continuous monitoring of electrocardiograph (ECG) and $S\text{po}_2$ were performed together with noninvasive blood pressure and central venous pressure (CVP). Over the next 12 h the thiopentone infusion rate was reduced and the convulsions did not recur. A total dose of thiopentone 1.4 g in 24 h was given. The patient remained haemodynamically stable and the blood gases on IPPV at an $F\text{IO}_2$ 0.6 were: pH 7.34, $P\text{O}_2$ 24.48 kPa, $P\text{co}_2$ 5.27 kPa, BE -4.7 mmol.l^{-1} and $S\text{ao}_2$ 97%. At this stage chest X ray, haematological and biochemical investigations and fundoscopy of the eye were all normal. The patient was gradually weaned from the ventilator and removal of the tracheal tube took place at 70 h after admission, when the patient was fully conscious. She became clinically jaundiced on the third day with abnormal liver function tests (total serum bilirubin 54.7 μmol.l^{-1}, conjugated bilirubin 17.1 μmol.l^{-1}, serum alanine aminotransferase 65 iu.l^{-1} and prothrombin time 22 s, which was twice that of the control value). At this stage the patient had developed a sensory deficit of the glove and stocking type with reduced muscle power (3/5) in

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all limbs. Vitamin K_1 10 mg was given together with glucose, potassium and insulin for nutritional support. By the fifth day the patient was fully oriented, the sensory deficit and muscle power were improving but the liver function tests were still abnormal (total serum bilirubin 27.3 μmol.l^{-1}, conjugated bilirubin 13.6 μmol.l^{-1} serum alanine aminotransferase 40 iu.l^{-1}). The prothrombin time was normal. Muscle power and liver function tests returned to normal by the 10th day but a sensory deficit to fine touch persisted until the 14th day. Spontaneous abortion occurred and dilatation and curettage was performed under local anaesthesia.

Case 2

A 22-year-old man was admitted unconscious to the critical care unit with a history of convulsions at home. He had consumed about 5.0 g of INH, with the intent of committing suicide. His protective airway reflexes were impaired but clinical examination was otherwise normal. After preoxygenation, tracheal intubation was performed with a cuffed tube and IPPV ($F\text{io}_2$ 1.0) was started. The patient developed generalised convulsions, for which diazepam 5 mg was given. Gastric lavage was performed and blood samples were sent for analysis. The arterial blood gas analysis showed pH 7.20, $P\text{O}_2$ 11.7 kPa, $P\text{co}_2$ 4.2 kPa, BE − 13.0 mmol.l^{-1} and $S\text{ao}_2$ 98%. The convulsions stopped, only to recur within a few minutes. Thiopentone 250 mg was given and a 0.1% infusion was started at a rate of 2 mg.kg^{-1}.h^{-1} together with an intravenous infusion of pyridoxine 5 g in 5% dextrose.

Continuous ECG and $S\text{po}_2$ monitoring were undertaken, while CVP and noninvasive blood pressure were measured at frequent intervals. The $F\text{io}_2$ was reduced to 0.5 and further arterial blood gas analysis showed the persistence of a moderate metabolic acidosis. The serum INH level was 184.5 μg.ml^{-1} while a full blood count, blood biochemistry and liver function tests were within normal limits (Table 1). Chest X ray and examination of the optic fundi did not reveal any abnormality.

The thiopentone infusion was gradually tapered off over the next 24 h (total dose of thiopentone 1.7 g) and IPPV was continued using the assist/control mode. Arterial blood gases at $F\text{io}_2$ 0.4 were normal. The patient was gradually weaned off the ventilator and the trachea extubated 72 h after admission.

Serum INH levels were serially monitored and there was marked improvement in the level of consciousness as blood levels of isoniazid decreased (Table 1).

On the fourth day, clinical jaundice appeared and a motor deficit in both upper limbs (power 3/5) was noted. Vitamin K_1 10 mg intramuscularly was started because of a prolongation of the prothrombin time (Table 1). The motor deficit and liver function tests had returned to normal by day 7 and INH was no longer detectable in the blood by day 8. Fundoscopy, visual acuity and visual evoked responses did not reveal any evidence of optic neuritis and the patient was discharged, symptom free, after 2 weeks.

Discussion

Isoniazid, the hydrazide of isonicotinic acid, is a first line drug in the treatment of tuberculosis [2]. It is well absorbed from the gastrointestinal tract and easily crosses tissue barriers to enter cells and cerebrospinal fluid (CSF). Peak plasma concentrations of 3–5 μg.ml^{-1} occur 1 to 2 h after oral ingestion of therapeutic doses. Concentrations in the CSF are similar to those in the plasma. In the presence of normal renal function 75–95% of isoniazid is excreted within 24 h, mostly as metabolites. The main excretory products result from enzymatic acetylation and hydrolysis [2]. However, there are great differences in the rates at which individuals acetylate isoniazid and this is genetically determined. There are slow acetylators and fast acetylators; in the former group the plasma half life of isoniazid is 2.5 to 3 times that in fast acetylators (140 to 200 min as opposed to 45–80 min). Sixty percent of Asian Indians are slow acetylators [4], hence the problem of isoniazid overdose in the Indian population is compounded.

Isoniazid toxicity produces the clinical triad of recurrent seizures refractory to standard anticonvulsant therapy, a metabolic acidosis resistant to treatment with sodium bicarbonate and coma. Acute ingestion of 2–3 g of INH can cause acute toxicity whilst 80–150 mg.kg^{-1} is associated with a high mortality rate [3]. Both of our patients developed the clinical triad of isoniazid overdose.

Table 1. Plasma isoniazid levels and liver function tests related to clinical events during the recovery phase in patient 2.

		Liver function tests			
Day	INH level (μg.ml^{-1})	S. Bil. (μmol.l^{-1})	ALT (IV.l^{-1})	PT (s)	Clinical event
1	184.5	17.1	25	14	Coma, convulsions ventilatory insufficiency
2	62.4	20.5	30	15	Semiconscious
3	16.5	34.2	56	16	Conscious, spontaneous respiration
4	9.6	61.5	106	17	Fully oriented, jaundice, muscle weakness
5	4.2	37.6	76	16	
6	3.5	30.7	46	14	Anicteric
7	0.8	13.6	28	12	Muscle power normal

INH, isoniazid; S. Bil., serum total bilirubin; ALT, alanine aminotransferase; PT, prothrombin time.

Isoniazid induces pyridoxine deficiency by increasing renal excretion of pyridoxine and by competitive inhibition of pyridoxine-kinase, the enzyme that converts pyridoxine to pyridoxal phosphate, which is physiologically active. This leads to decreased brain gamma-aminobutyric acid (GABA) levels, which is probably responsible for the severe, recurrent seizures, peripheral neuropathy (usually affecting pain, touch and temperature), motor involvement with muscle weakness and optic neuritis. Isoniazid also inhibits the conversion of lactate to pyruvate. This, together with the seizure-induced tissue hypoxia, causes a severe anion gap metabolic acidosis (anion gap > 12 mmol.l^{-1}) and increased serum lactate levels (9 to 16 mmol.l^{-1}) [3]. Hepatic dysfunction occurs secondary to production in the liver of acetylhydrazine, a chemically active metabolite of isoniazid. It ranges from mild (some elevation of hepatic enzymes and prolongation of prothrombin time) to a severe hepatitis, with a mortality of 20%. Isoniazid, if administered during pregnancy [3], appears in fetal blood.

The management of patients with acute isoniazid poisoning is aimed at gut decontamination, control of convulsions, correction of tissue hypoxia and administration of pyridoxine [5]. Isoniazid is known to inhibit parahydroxylation of phenytoin, therefore phenytoin toxicity may occur [2], which limits its rôle in the treatment of acute INH poisoning. Isoniazid-induced seizures are refractory to usual anticonvulsants therefore thiopentone is preferred [5]. Pyridoxine, which is a specific antidote, is administered intravenously in a dose of 1 g for each gram of isoniazid ingested [3]. In INH overdose up to 52 g of intravenous pyridoxine has been tolerated without adverse effect [6]. Haemodialysis and exchange transfusion have rarely been used but may be effective [3], although, maintenance of an adequate urine output is usually sufficient for drug elimination [3].

Serum INH levels should be closely monitored to guide the management. These could not be performed in the first patient but in the second case they were monitored serially by fluorimetric assay [7]. On admission the serum INH level was 184.5 μg.ml^{-1} (a level of 150 μg.ml^{-1} has been reported to be fatal). A metabolic acidosis persisted until levels were below 62.4 μg.ml^{-1}. It is interesting to note that from day 1 to day 4, when the INH levels were decreasing the hepatic enzymes continued to increase (Table 1). This probably indicates that the hepatitis-like reaction associated with isoniazid is unrelated to dose and may occur even after elimination of drug [4], possibly due to production of an active metabolite in the liver. Serum INH levels as low as 9.6 μg.ml^{-1} were still associated with a motor deficit and muscular weakness. Even on the sixth day the levels were still within the therapeutic range (3–5 μg.ml^{-1}). This suggests that the patient was a slow inactivator of INH, which is commonly seen in the Indian population.

Acute isoniazid poisoning presenting with severe, recurrent seizures and coma can be successfully treated with ventilatory support, barbiturates and pyridoxine therapy. The measurement of serial INH levels may provide an important guide to the management of these patients.

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CASE REPORT

Prolonged resuscitation in acute deep hypothermia

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Summary

A case report is described with successful outcome of prolonged cardiopulmonary resuscitation in a 30-year-old man suffering from acute deep hypothermia. His lowest temperature recorded was 23°C. Continuous external cardiac massage was required for a total of 4.5 h whilst rewarming was instituted. The patient eventually left hospital with no permanent sequelae. A review of hypothermia follows, emphasising some important management principals and pitfalls.

Key words

Hypothermia; accidental.
Resuscitation; cardiopulmonary.

Case history

A 30-year-old man was rescued from sea water in early February 1991 where he was clinging to a sea wall ladder, calling for help. The ambient air temperature was −6.5°C, sea temperature was 0°C.* He collapsed on being pulled from the water and by the time the ambulance crew arrived he was pulseless. External cardiac massage and oxygen by face mask were administered during transit to hospital. On arrival at the accident and emergency department, his rectal temperature was 28°C and the electrocardiograph (ECG) showed ventricular fibrillation (VF). Defibrillation was attempted three times in the accident and emergency department without success. His trachea was intubated and his lungs ventilated, and he was given intravenous adrenaline and lignocaine. The ECG then changed to asystole and his rectal temperature was found to have decreased further to 23°C. Adrenaline produced a return to coarse VF and the patient was transferred to the intensive care unit with cardiopulmonary resuscitation in progress. On arrival his core temperature had stabilised at 23°C, his pupils were fixed, dilated and nonreacting and he was in coarse VF. Cardiopulmonary resuscitation was continued whilst the patient was rewarmed.

Active rewarming was commenced with electric blankets, warmed intravenous solutions and ventilation with heated-humidified gases. Manual external cardiac massage was continued by operating department assistants working in relay. A catheter was inserted in the right radial artery. Arterial and central venous blood pressures (CVP) were monitored. The efficacy of external cardiac massage was judged from the mean pressures obtained from the arterial pressure transducer, and the technique adjusted accordingly. The use of pulse oximetry was abandoned as the readings were considered unreliable. The bladder was catheterised. Arterial blood gases, haematology and biochemistry were monitored and revealed an initial profound metabolic acidosis (Tables 1, 2 and 3). Routine drug screening was performed, and was negative.

The core temperature started to increase after one hour and thereafter at approximately 1°C.h^{-1}. Spontaneous cardiac activity (sinus bradycardia of 40, arterial blood pressure 70/20 mmHg) returned at a core temperature of 27.2°C, after 4.5 h of continuous external cardiac massage.

Adrenaline was commenced at 1 μg.kg^{-1}.min^{-1} and the systolic pressure increased to 115 mmHg over the next hour. Dopamine was started at 2.5 μg.kg^{-1}.min^{-1} to maintain urine output. A 'cerebral salvage' routine of intermittent positive pressure ventilation (IPPV), mannitol and methylprednisolone was used for the first 24 h. Fresh frozen plasma (6 units) and platelets (6 units) were transfused to correct a thrombocytopaenia of 54×10^9.ml^{-1}, although at no time was there overt bleeding. The patient's urine myoglobin was negative.

The patient reached normothermia 12 h after admission. At this point his arterial blood pressure was 100/50 mmHg with a CVP of +10 cmH$_2$O. Blood gases were in the normal range with an $F\text{io}_2$ of 70%. There was a standard

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*Data from Plymouth Meteorological Office

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Table 1. Haematology.

Time (h)	Temperature (°C)	Haemoglobin ($g.l^{-1}$)	Haematocrit (%)	White cell count ($x10^6.ml^{-1}$)	Platelets ($x10^9.ml^{-1}$)	INR (ratio)	APTT (ratio)
1	23.0	133	40.8	8.60	121	—	—
2	23.5	106	30.9	7.62	54	1.9	1.3
6	28.0	114	31.7	6.71	178	1.5	1.1
12	37.4	119	33.9	10.5	223	—	—
24	38.0	87	25.2	11.8	146	1.5	1.1
36	37.9	108	29.9	16.2	176	—	—
48	37.2	98	29.2	17.6	147	1.4	1.1
72	38.0	102	30.6	16.7	113	1.4	1.1
96	37.1	110	32.9	12.7	143	1.4	1.0
120	36.9	113	32.2	12.9	201	1.2	1.0
144	36.8	119	34.5	11.9	326	—	—

NB: Fibrin degradation products were only detected at 24 h ($40 < FDP < 80\ \mu g.ml^{-1}$).
INR, international normalised ratio; APPT, activated partial thromboplastin time.

Table 2. Biochemistry.

Time (h)	Na^+ ($mmol.l^{-1}$)	K^+ ($mmol.l^{-1}$)	Urea ($mmol.l^{-1}$)	Creatinine ($\mu mol.l^{-1}$)	Glucose ($mmol.l^{-1}$)	Protien ($g.l^{-1}$)	Albumin ($g.l^{-1}$)	Bilirubin ($\mu mol.l^{-1}$)	AST ($u.l^{-1}$)	GGT ($u.l^{-1}$)	ALP ($u.l^{-1}$)
1	146	4.0	6.2	94	9.9	60	42	7.0	—	12	182
2	143	3.6	6.4	93	7.9	39	27	8.0	475	19	127
6	142	2.7	7.6	100	14.3	60	44	—	—	—	—
12	141	3.2	7.8	94	10.2	59	44	—	—	—	—
24	141	3.9	8.6	89	6.3	58	45	28.0	1531	35	133
48	137	4.4	9.9	59	6.3	56	44	6.0	1185	26	136
72	140	4.1	5.7	64	7.8	54	44	16.0	1686	31	139
96	139	4.3	4.1	81	10.5	62	45	18.0	1046	34	160
120	136	4.5	4.5	51	5.9	60	42	18.0	562	36	168

AST, aspartate aminotransferase; GGT, gamma glutamyl transpeptidase; ALP, alkaline phosphatase.

Table 3. Blood gases/acid-base balance. All values are corrected for temperature.

Time (h)	Temperature (°C)	FIO_2 (%)	PEEP (cm)	PaO_2 (kPa)	SaO_2 (%)	$PaCO_2$ (kPa)	pH	Standard bicarbonate ($mmol.l^{-1}$)	Base excess ($mmol.l^{-1}$)
1 (CPR)	23.0	100	0	8.7	96	2.0	7.22	9.1	−20.7
2 (CPR)	23.5	100	0	43.2	99	1.2	7.28	8.5	−22.3
3 (CPR)	24.0	100	0	21.1	99	1.5	7.20	7.9	−23.1
	(HCO_3 given)								
4 (off IPPV)	25.2	100	0	35.8	99	3.5	7.61	30.2	+6.7
5	26.5	100	0	43.6	99	3.5	7.39	18.8	−7.8
6	28.0	100	0	37.4	99	2.2	7.56	19.8	−6.8
8	32.0	40	0	6.9	94	3.6	7.48	22.6	−2.3
	(HCO_3 given)								
10	35.5	70	0	15.7	99	5.1	7.50	30.5	+6.7
12	37.4	75	0	11.0	97	5.5	7.48	30.2	+6.4
18	38.1	50	0	9.6	95	4.3	7.53	28.7	+4.2
24	38.0	50	0	10.6	96	4.5	7.46	25.3	+0.6
36	37.9	60	2	9.2	94	4.65	7.45	24.8	+0.3
48	37.2	60	0	11.4	95	6.4	7.33	23.7	−0.5

PEEP, positive end-expiratory pressure; $PaCO_2$ arterial carbon dioxide tension; CPR, cardiopulmonary resuscitation; IPPV, intermittent positive pressure ventilation.

base excess of $+7\ mmol.l^{-1}$, probably due to the earlier administration of bicarbonate. Chest X ray demonstrated a left pneumothorax which was drained with an apical drain.

The patient remained generally stable, and at 24 h after normothermia had been attained, neurological assessment indicated no focal or global deficit. Ranitidine, cefuroxime morphine and pancuronium were administered intravenously. Ventilatory support was continued for a total of 48 h until the patient was fully conscious and cooperative, at which point his trachea was extubated. An FIO_2 of 60% with continuous positive airway pressure (CPAP) was required for the next 72 h to maintain blood gases within normal limits.

Electrocardiographs at normothermia were consistent with an acute anterior myocardial infarct. However, there were no specific isoenzyme changes and follow-up echocardiography showed no wall motion abnormality.

Over the ensuing days, gas exchange gradually improved and the pneumothorax resolved. All measurements returned towards normal. The patient was discharged 5 days after admission with no apparent permanent disability. He admitted to a past history of psychiatric treatment for depression and that this had been a determined suicide attempt.

Discussion

This patient was suffering from acute deep hypothermia [1, 2] which was associated with the apparent complete absence of brain stem and cortical activity. A literature search has failed to reveal a longer duration of cardiopulmonary resuscitation in a hypothermic patient [3–6]. As in previous case reports of hypothermia, provided the history has been correctly obtained and the correct management protocols followed, full recovery may be possible.

The underlying pathogenesis of hypothermia is the predominance of heat loss over heat production, and the loss of compensating mechanisms [7–10] (Table 4). Decreased thermoregulation (e.g. general anaesthesia and burns) and decreased heat production (e.g. hypothyroidism) may be important predisposing factors. Water immersion is particularly important as it causes the very rapid onset of hypothermia due to heat loss by conduction, whereas heat loss by radiation which occurs predominately in exposure to air is a much slower process.

This case clearly demonstrated the phenomenon of postimmersion collapse. Despite being conscious in the water, the patient collapsed after being lifted out and then suffered a cardiac arrest. The cause of this postimmersion collapse is the loss of the hydrostatic support provided by water. Water effectively acts as an antigravity suit, and if immersion is prolonged, there may be a diuresis due to the increase in the central venous pressure as peripheral blood is forced into the central compartment. On being removed from the water, central venous pressure falls and there is therefore a decrease in arterial pressure which causes the collapse. Postimmersion collapse is well recognised and there are many anecdotal reports of it in survivors of immersion, including the Titanic disaster and the 1979 Fastnet tragedy. We believe that this is the first clearly witnessed and documented case of postimmersion collapse.

As the body temperature falls there is a complex progression of physiological responses. Initially, heat is generated by shivering and heat loss is reduced by peripheral vasoconstriction. There may be a progressive decrease in core temperature after removal from the thermal stress. This is the 'afterdrop phenomenon', which is caused by cold peripheral blood being returned to the core once local rewarming of the extremities has produced peripheral vasodilatation. The basal metabolic rate falls progressively and reaches 50% of normal at 28°C [11]. The stress response release of catecholamines and glucocorticoids inhibits insulin release and action. Glycogenolysis and gluconeogenesis are therefore stimulated, causing serum glucose to increase as the body cools. Hepatic glycogen stores may be depleted.

Table 4. Factors predisposing to acute deep hypothermia.

Environment	Behaviour	Drugs
Winter	Inadequate clothing	Alcohol
Latitude	Wet clothing	Nicotine
Windchill	Immersion	Sedatives
Waterchill	Prolonged exposure	Opiates
	Poor fitness	Phenothiazines
	Fatigue	
	Poor shelter	

There is an initial fall in plasma potassium due to entry into cells, followed by a rise as potassium is released from damaged and nonmetabolising cells. Plasma sodium, calcium and chloride levels are maintained until the temperature falls below 25°C.

Acid-base physiology in hypothermia is a complex subject, which is explained more fully in several review articles [12–14]. The pH of whole blood rises with falling temperature to 7.6 at 25°C. This is due to variation in the pKa of the most predominant buffer, the histidine–imidazole groups of haemoglobin. There are also changes in the measured $P\text{a}O_2$ and $P\text{a}CO_2$ both falling with temperature, and there has been controversy over whether corrected or uncorrected acid-base and gas estimations should be used in management of hypothermia. The blood–gas machine warms the blood to 37°C and provides an uncorrected value. Thus the default setting on the blood–gas machine assumes that the patient is normothermic. A corrected value can be obtained by keying in the actual body temperature. The corrected values obtained as a patient rewarms are difficult to interpret and acidosis is more easily detected with uncorrected values, which also allow reference to standard acid-base nomograms to evaluate mixed disturbances. In cardiac anaesthesia, some anaesthetists maintain corrected pH at 7.4 by adding carbon dioxide to the inspired mixture arguing that the respiratory acidosis that this produces is beneficial in increasing tissue oxygen unloading. The alternative is to maintain uncorrected blood gases to pH 7.4 and $P\text{a}CO_2$ 5.3 kPa, allowing the actual values to follow *in vitro* changes of blood. This is termed the ectothermic principle. The rationale for these two approaches is complex, but confusion is probably less likely if uncorrected values are used.

Disseminated intravascular coagulation was not a significant complication in this case, although it may be a feature in advanced cases [15].

All organ systems are affected by hypothermia. In deep hypothermia there is progressive coma and decrease in all central nervous system functions. Cerebral blood flow decreases by 6–7% for each degree drop in core temperature. The cerebral metabolic rate for oxygen ($CMRO_2$) is decreased once shivering has ceased at around 34°C [11]. At temperatures below this, the very low $CMRO_2$ allows the possibility of complete recovery despite prolonged cerebral anoxia.

In the cardiovascular system, cardiac function is depressed by low temperatures, but progressive slowing of the sinus nodal rate with cooling is masked early on by a sympathetic mediated tachycardia. Sinus bradycardia supervenes at 32°C and with further cooling ectopic atrial foci may be seen. Rhythm abnormalities are probably induced due to the existance of transmyocardial temperature gradients [16]. At approximately 30°C, atrial irritability may provoke atrial flutter or fibrillation. Ventricular irritability increases with further cooling and ventricular ectopics are followed by ventricular fibrillation. Asystole may supervene at very low temperatures as was seen in our patient.

Conduction disturbances accompany rhythm abnormalities [9] and there is prolongation of the PR, QRS and

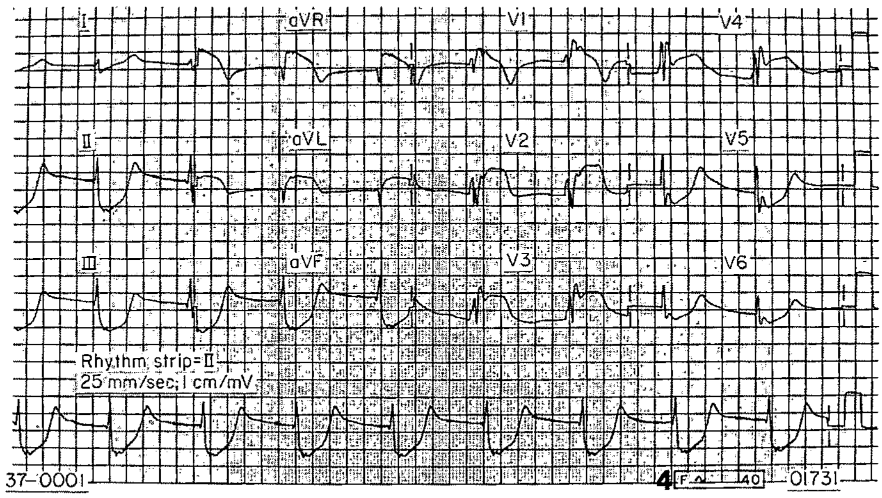

Fig. 1. The patient's ECG taken 6 h after admission during rewarming.

QT intervals. His bundle electrocardiography has demonstrated that there may be a conduction defect at the level of the AV node, which is fully reversible on rewarming [17]. A secondary deflection of the QRS complex, known as the J or Osborn wave [18], may occur at varying temperatures and is fully reversible. It is pathognomonic of the hypothermia syndrome if accompanied by a low core temperature, but has no prognostic significance. ECGs of this patient demonstrate the J wave whilst rewarming was taking place (Fig. 1).

Early ventilatory stimulation is followed by depression with further cooling. The anatomical deadspace is increased by 50% at 25°C secondary to an anticholinergic effect, and ventilation–perfusion abnormalities also contribute to an increase in physiological deadspace [19]. Aspiration pneumonia and near-drowning are also associated with immersion hypothermia, and oedema of the respiratory epithelium and cilial dysfunction may lead to respiratory infections in survivors. Adult respiratory distress syndrome is a recognised sequel in advanced cases.

In the kidney, there is a cold diuresis, due initially to peripheral vasoconstriction and then to decreased tubular metabolic activity. Acute tubular necrosis is a common feature of fatal cases of hypothermia [20].

The most important management principles are prevention and early recognition of the syndrome. Initial first aid treatment should involve careful removal of the patient from the source of the thermal stress. If the case is due to immersion in water, the patient should be kept horizontal to minimise the postimmersion cardiovascular collapse. The airway must be secured and a suction catheter passed if there is suspicion of aspiration. Cardiopulmonary resuscitation should be instituted immediately if necessary, and continuously applied until the cardiac output returns spontaneously or cardiopulmonary bypass is instituted. This may be for a period of some hours, as was the case in our patient. An admission drug screen should be performed because of the association of hypothermia with drug intoxication.

Management

Treatment of acute, deep hypothermia should be carried out in an intensive therapy unit with full invasive monitoring. Defibrillation should be avoided below 30°C because of the myocardial damage which may be sustained by direct current below this temperature [16]. In deep hypothermia, active rewarming should be commenced as soon as possible aiming at a rate of 1–2°C h^{-1} to avoid the cardiovascular instability that may be associated with more rapid rewarming techniques [14]. Conventional conservative measures, which were successfully used in our patient, include the use of warming blankets, warmed intravenous fluids and heated, humidified inhaled gases [21, 22]. Some centres have used invasive measures including peritoneal lavage [23, 24], pleural lavage [25, 26] and cardiopulmonary bypass [3, 4, 27, 28] with little or no apparent improvement in eventual survival rates. In one reported patient, who presented twice within 25 days with deep hypothermia, there was no difference in outcome between treatment with active and passive rewarming [22].

The method of rewarming seems to be less important than its efficient application in combination with effective cardiopulmonary resuscitation and maintenance of metabolic, haematological, cardiovascular and respiratory homeostasis. Despite recently expressed views [29, 30], the authors believe that patients may be successfully managed without invasive rewarming techniques such as cardiopulmonary bypass or peritoneal dialysis if such facilities are not immediately available.

In an effort to identify those patients likely to survive and therefore those who receive maximal care, some workers have looked at outcome scores of hypothermia and prognostic factors in outcome [31–33]. Marked hyperkalaemia, intercurrent medical illness, and the existence of disseminated intravascular coagulation have all been suggested as poor outcome indicators. However, in the opinion of the authors, this is of very limited practical use. Maximal efforts at resuscitation should be made until normothermia is achieved. Only then should a decision to abandon resuscitation be made.

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CASE REPORT

Does hypothermia protect against the development of hepatitis in paracetamol overdose?

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Summary

A 24-year-old female presented in hospital following self-poisoning with a dose of greater than 30 g of paracetamol (acetaminophen), taken both as co-proxamol (dextropropoxyphene and paracetamol) and paracetamol. She arrived in hospital more than 18 h after ingestion of the drug. On admission, she was profoundly hypothermic, with a rectal temperature of 19°C. Her paracetamol level was 943 μmol.l^{-1} which, when related to the time of ingestion, implied a very high risk of hepatocellular damage as well as fulminant liver failure, even if she was treated with the antioxidant n-acetylcysteine. The patient's condition was stabilised by initial resuscitation with fluids, vasoactive drugs, and active rewarming. N-acetylcysteine therapy was begun promptly. This patient's liver function tests remained entirely normal in spite of the delay in presentation and she made a rapid and complete recovery. This remarkable clinical course indicates a possible role for therapeutically induced hypothermia in the management of severe paracetamol overdose, particularly in the group of patients who seek medical attention some hours after ingestion of the drug and who therefore remain at high risk, despite treatment with n-acetylcysteine.

Key words

Toxicity; paracetamol.
Complications; hepatic.
Hypothermia.

As many as 200 deaths per year in the UK are caused by paracetamol ingestion [1], and paracetamol poisoning is the most frequent cause of fulminant hepatic failure in the UK [2]. Patients who ingest large amounts of paracetamol and present at hospital late, beyond the time for effective protection by intravenous n-acetylcysteine [3], remain a difficult management problem and represent a large proportion of the patients who require intensive care for the management of fulminant hepatic failure and liver transplantation.

The present patient's clinical course may point to a potential advance in the care of patients suffering from paracetamol poisoning.

Case history

A 24-year-old female presented to the accident and emergency department in deep coma. The brief history obtained from a relative revealed a manic-depressive illness, previous episodes of self-poisoning and a disagreement, involving physical violence, 24 h before, which could have precipitated the attempted self-poisoning.

On examination, the patient was found to be profoundly hypothermic with a rectal temperature of 19°C. Although severely hypothermic, she still maintained a heart rate of 30–40 beat.min^{-1} and her electrocardiogram showed an irregular broad–complex bradycardia with 'J' waves. She was hypotensive with blood pressure of 50/30 mmHg. She was still breathing spontaneously but was hypoventilating and cyanosed. Neurological examination revealed fixed dilated pupils, a Glasgow Coma Scale of 5 and generally increased muscle tone. No gag reflex was elicited. Blood gases revealed a respiratory acidosis. There was mild hyperkalaemia (5.9 mm.l^{-1}) and mild hyperphosphataemia (2.63 mmol.$^{-1}$), consistent with hypothermia. Haematological and coagulation studies were normal. The serum paracetamol level was 943 μmol.l^{-1}. No salicylate was detected. The diagnosis of paracetamol poisoning was

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Table 1. Biochemical and haematological parameters including liver function tests, following admission with paracetamol poisoning.

	Day				
	1	2	4	5	6
Sodium; mmol.l^{-1}	132.0	140.0	141.0	141.0	
Creatinine; μmol.l^{-1}	63.0	71.0	58.0	59.0	
Pao$_2$; kPa (Fio$_2$)	46* (1.0)		11.0 (0.38)		13.0 (0.21)
Paco$_2$; kPa	9.7	4.8	—	4.8	
pH	7.13	7.44	—	7.45	
Base excess; mmol.l^{-1}	−3.0	−1.0	—	2.0	
Alanine aminotransferase; U.l^{-1}	—	—	—	27.0	19.0
Gamma glutamyltransferase; U.l^{-1}	—	—	27.0	18.0	
Alkaline phosphatase; U.l^{-1}	23.0	44.0	56.0	53.0	
Bilirubin; μmol.l^{-1}	10.0	11.0	11.0	9.0	
Prothrombin time > control; s	5.0	1.0	0.0	2.0	

*The patient was undergoing intermittent positive pressure ventilation because she was admitted in respiratory failure.

made, together with that of profound hypothermia, which was probably also drug related.

Initial resuscitation included tracheal intubation and positive pressure ventilation. The administration of 1200 ml of colloid, and intravenous adrenaline (20 ml adrenaline 1 in 10 000), isoprenaline (600 μg total by intravenous infusion), and ephedrine (60 mg in ten 6 mg increments) was required to increase the heart rate to 65 beat.min^{-1} and the blood pressure to 90/50 mmHg. Naloxone (1.2 mg) and flumazenil (200 μg) were also given. Active core rewarming was begun with an intravenous infusion of 10% glucose at 37°C. Treatment with n-acetylcysteine ('Parvolex', Duncan, Flockhart & Co.) was initiated promptly on receipt of the serum paracetamol level, (approximately 19 h after ingestion of the paracetamol), starting with 10 g dose in 500 ml of 5% glucose given over 5 h.

Within 2 h the rectal temprature was 27°C. Gradual rewarming was continued using an insulating blanket and warmed humidified gases. Cimetidine was also given to prevent gastrointestinal haemorrhage and in the hope of reducing hepatocellular damage. The total dose of n-acetylcysteine given intravenously was 23 g over 21 h. Rewarming was accompanied by large electrolyte shifts which necessitated replacement of 140 mmol of potassium chloride during the 12 h period of rewarming. In addition, hypoglycaemia occurred as the body temperature rose, and was treated with 50 ml of 50% glucose intravenously on two occasions.

Twelve hours following her arrival in hospital, the patient was normothermic, moving all limbs, responding to commands and able to breathe spontaneously. She confirmed that she had ingested tables: 100 co-proxamol tablets (dextropropoxyphene hydrochloride 32.5 mg and paracetamol 325 mg), 100 prothiaden (dothiepin hydrochloride) tablets, and some additional paracetamol tablets, about 18 h before admission to hospital.

Liver function was monitored throughout the patient's stay in hospital. On day 4 (when hepatic damage is usually maximal following a large paracetamol overdose), the prothrombin time, (which is used to predict the likelihood of requiring liver transplantation [4]), was 15 s with a control of 14 s. The plasma bilirubin was never elevated. Alanine aminotransferase was normal at 27 mmol.l^{-1}.

At all times, the measured indices of liver function remained normal, showing no evidence of hepatocellular injury. The patient made a full recovery.

Discussion

Paracetamol, in a dose greater than 15 g, produces hepatocellular damage because the paracetamol is metabolised by the hepatic P450IIE and P4501A2 enzymes to form a reactive intermediate n-acetyl-p-benzoquinonimine [5,6]. This free radical is normally rapidly inactivated by conjugation with glutathione, but when a large excess of paracetamol is present this pathway becomes saturated. Hepatocellular toxicity can be lessened by supplying an alternative source of sulphydryl groups, in the form of n-acetylcysteine, to bind the reactive metabolite.

The management of paracetamol poisoning depends on the identification of patients at risk of developing hepatocellular damage. A graph relating circulating paracetamol concentration to time of ingestion is used to identify patients who are defined as being at 'probable risk', and 'high-risk' [7,8]. The present patient's circulating paracetamol concentration 943 μmol.l^{-1} 18 h after ingestion of the drug placed her in the 'high-risk' category.

The most useful prognostic indicators of probable requirement for liver transplantation in patients who have ingested paracetamol include pH < 7.30, prothrombin time > 100 s, and serum creatinine > 300 μmol.l^{-1} [9]. In this patient, prothrombin times showed no significant increase; an initial arterial pH of 7.19 was attributable to hypoventilation and was corrected by mechanical ventilation; and blood creatinine concentrations were normal throughout the clinical course (Table 1). These results were very unusual for a patient in the 'high risk' group.

Prescott *et al.* [10] found severe liver damage in 85% of 'high risk' patients treated with n-acetylcysteine 15–24 h after ingestion of the drug, and an incidence of 93% with hepatic damage in a similar group given only supportive therapy. The latter author concluded that n-acetylcysteine did not confer protection 15 h after paracetamol ingestion. However, his conclusion is controversial. A recent study by Harrison and his colleagues at the King's College Hospital

Liver Unit indicated that late treatment with n-acetylcysteine was more effective than simple supportive therapy, both in reducing mortality (37% vs 58%), and in preventing progression to Grade III/IV hepatic coma (51% vs 75%) [11]. They also studied patients already in established hepatic failure [12] and showed improved survival (48% vs 20%) in the group treated with n-acetylcysteine. However, both studies concluded that, although the eventual outcome was improved, n-acetylcysteine did not prevent hepatitis or severe deterioration of liver function. Our patient did not follow the predicted serious clinical course. Despite evidence that n-acetylcysteine is useful even when given late in the treatment of paracetamol poisoning, it is unlikely that its administration in this patient was responsible for the total absence of hepatocellular damage.

Hypothermia is not a usual feature of paracetamol poisoning, and in this patient it was probably caused by loss of consciousness, together with the low environmental temperature and the ingestion of other tablets. The episode of self-poisoning occurred during February in Scotland and central heating was not in use when the patient was found. It has been shown in healthy volunteers wearing light indoor clothing, that core temperature decreases by 0.4 degrees C per hour when lying on the floor in a cold environment, despite the metabolic rate being doubled [13]. When compensatory responses are attenuated, as in this case, body temperature may decrease considerably. The opioid component of co-proxamol was probably in part responsible, by producing central depression of conscious level and hypothalamic temperature regulation [14]. Central effects of dothiepin probably also contributed to the decrease in body temperature. This combination of factors resulted in hypothermia, which appears to have exerted a strongly protective effect, as shown by the absence of hepatocellular dysfunction.

Induced hypothermia is used routinely during cardiopulmonary bypass [15] because it results in decreased cellular metabolism and a lower oxygen requirement, thereby reducing the risk of hypoxic damage [16]. There are many documented cases of survival following prolonged cardiorespiratory arrest during hypothermia, which have been attributed to reduced oxygen demand in the hypothermic state [17]. Hepatocellular metabolism, including conjugation, has been shown to be depressed by hypothermia [18].

The high paracetamol level and the late intervention in this patient placed her at high risk of hepatitis and fulminant hepatic failure. We therefore postulate that a reduction in hepatocellular metabolism secondary to hypothermia may have attenuated the toxic effects of the large dose of paracetamol, thereby preventing hepatitis.

In the light of this case we suggest that some patients with severe paracetamol poisoning may benefit from induced hypothermia, in an attempt to reduce the incidence and severity of liver damage.

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SPECIAL COMMUNICATION

Managing the airway in cervical spine injury

A review of the Advanced Trauma Life Support protocol

P. R. WOOD AND P. G. P. LAWLER

Summary

The American College of Surgeons' Advanced Trauma Life Support protocol for managing the airway in patients with a cervical spine injury is reviewed. The relative risks and benefits of oral and nasotracheal intubation are discussed and the potential hazards of alternative methods of airway control are considered with particular respect to British practice.

Key words

Anaesthesia; trauma.
Airway; cervical spine injury.

The incidence of cervical spine injury in patients who have sustained major trauma is between 1.5 and 3% [1,2]. The incidence is higher in association with high-speed road traffic accidents or head-first falls [1,3]. All such injuries may require immediate measures to ensure airway control. Neurological deficit occurs in 40% of cervical spine injuries, most often from fracture dislocations [4]. As many as 10% of patients may suffer increased neurological deficit after cervical spine injury [5].

An actual or suspected cervical spine injury must not delay resuscitation, but the fear that manipulation of the head and neck may precipitate a neurological disaster has created continuing controversy regarding the appropriate methods of airway management.

Current guidelines

The Advanced Trauma Life Support (ATLS) course has been operational in the United States since 1979. This course teaches a didactic system of care for the initial treatment and stabilisation of the trauma patient. The practical details found in the ATLS manual [6] represent a consensus of opinion from an advisory body (the Committee on Trauma) of the American College of Surgeons. The course is designed particularly for emergency room physicians, who, outside a tertiary level trauma centre, will be responsible for the initial care of trauma victims. The impact of ATLS teaching is considerable and increasingly relevant to UK practice since its adoption by the Royal College of Surgeons of England [7].

ATLS protocol

The management of the airway as taught by the ATLS has historically been biased towards a surgical approach. Current recommendations for an unconscious victim of blunt trauma who requires advanced life support are [6]: (1) Apnoeic patient (no X ray studies). Oral tracheal intubation. If unable, establish a surgical airway (= tracheostomy or equivalent). (2) Spontaneously breathing patient (time for X ray). If cervical spine injury excluded proceed with oral tracheal intubation. If cervical spine injury confirmed, attempt blind nasotracheal intubation. If unable, perform orotracheal intubation or surgical airway. (3) Spontaneously breathing patient (no time for X ray). Blind nasotracheal intubation. If unable, proceed with orotracheal intubation or establish surgical airway.

Despite modification (before 1984, even greater reliance was placed on surgical approaches) there is an implicit acceptance that in the presence of suspected or actual cervical spine injury, orotracheal intubation is intrinsically dangerous. However, if the studies of airway management in cervical spine injury are examined critically it is clear that this argument is unsubstantiated.

Radiological assessment

X ray examination has several limitations. Immediate airway control may be required before radiological assessment, or only a single cross-table lateral film may be available. The inadequacy of the lateral view in screening

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cervical spine injury is well established [8,9]; using plain films, radiological evidence of trauma may be absent in 17% of patients with neurological injury [4]. Finally, static, nonfluoroscopic images cannot accurately predict the effect of a subsequent airway manoeuvre.

The effect of therapeutic manoeuvres upon cervical spine injury

The immobilisation of an actual or suspected cervival spine injury is an important first step in management. Podolsky *et al.* [10] studied the effect of six commonly used immobilisation devices on cervical spine movement in normal volunteers. The use of bilateral sand-bags with 3-inch forehead tape provided the best method of limiting flexion, extension, rotation and lateral bending. Further significant reduction in extension was achieved by addition of a two-peice, semi-rigid Philadelphia collar. This combination provides almost total immobilisation.

Majernick *et al.* [11] studied cervical spine movement with orotracheal intubation and found that while movement occurred in all cases it was minimised by an assistant applying 'in-line stabilisation'. The paper does not explain how this was done. Manually restraining the head in a neutral position to prevent active flexion/extension is a different manoeuvre from the application of axial traction (by weights or bodily force), yet the literature on airway management in cervical spine injury is complicated by repeated failure to define exactly how cervical stabilisation is achieved. The ATLS instructions [6] refer to an assistant applying 'manual in-line immobilisation', but fail to explain how to achieve this.

Direct laryngoscopy and orotracheal intubation

Successful orotracheal intubation depends on flexion of the neck and extension at the atlanto-axial joint. Considerable neck movement may be required to create satisfactory alignment of the oral–pharyngeal–laryngeal axis.

The disposition of the cervical vertebrae has been studied radiologically in healthy volunteers during laryngoscopy [12]. The authors noted that the standard intubating position (defined in the study) was associated with relatively horizontal cervical vertebrae, with increasing extension from C_4 to C_1, becoming maximal at the atlanto-axial complex. These findings of relative stability in the lower cervical spine may be important in airway management, as the majority of injuries occur between C_3 and C_7 [13].

Bivins *et al.* [14] studied victims of blunt traumatic cardiac arrest in whom resuscitation failed. Using a series of cervical spine X rays they followed the radiological appearance of orotracheal intubation during the application of 21.8 kg of bidirectional axial traction (15 kg to depress the shoulders, 6.8 kg head traction). Four subjects had an unstable injury (one $C_{6\text{–}7}$ fracture dislocation, one Hangman's fracture and two atlanto-occipital dislocations) and in this group intubation with traction produced unacceptable distraction (mean 7.75 mm) at the injury site. In three of the four cases, subluxation also occurred. The application of traction alone also produced abnormal movements in the unstable injuries. The authors concluded that if urgent intubation is required in trauma patients before definitive cervical spine X rays have been taken, the nasal route should be used, with the head and neck held in a neutral position, and without axial traction.

Aprahamian *et al.* [15] studied a fresh cadaver model in which a complete C_5–C_6 ligamentous instability was created surgically. Cervical spine X rays were used to study the effects of chin lift, jaw thrust, head tilt, airway insertion and oro- or nasotracheal intubation. They found that any manoeuvre which created extension of the head on the neck produced anterior subluxation and widening of the disc space at the level of injury. Increase in disc space was least affected by the use of an oral or nasal pharyngeal airway (2 mm) but the chin lift and jaw thrust manoeuvres were particularly hazardous ($>$ 5 mm). Orotracheal intubation produced intermediate changes (3–4 mm) in disc space, while blind nasotracheal intubation produced up to 2 mm of posterior subluxation, but no increase in disc space. The manoeuvres were repeated while stabilising the neck with either a soft or a Philadelphia collar. These devices had no consistent effect, producing a worsening of instability in some instances. The authors concluded that orotracheal intubation produced potential aggravation of the injury while stability was maintained with use of either a nasal airway or nasotracheal tube. Both studies have been criticised in various respects, including small numbers, nonapplicability to the living patient, and failure to standardise the 'intubating force'.

Rhee *et al.* [16] reported the airway management of 17 patients with cervical spine injury in whom oral intubation was performed with cervical immobilisation (not defined) in the emergency room. There were no apparent neurological sequelae. The difficulties of documenting change in neurological status in this setting is a limitation of the study, but of the 17 patients, 10 had no deficit before or after intubation.

Stellin *et al.* [17] failed to find any change in pre- and postintubation neurological status in 31 cervical spine injury patients in whom orotracheal intubation was performed with 'manual in-line traction'. Their description suggests in-line stabilisation without active traction, but this is not clear.

Extensive clinical experience has been described from the Maryland Shock Trauma Centre [18], where orotracheal intubation has been employed successfully on more than 3000 trauma patients with suspected cervical spine instability. Thirty patients were proved subsequently to have a cervical spine injury but none developed changes in spinal cord function during intubation. The Maryland clinicians accept that there is difficulty in defining cervical stabilisation which may include active axial traction or neutral immobilisation [19]. They emphasise the importance of ensuring oxygenation by bag–mask ventilation with cricoid pressure before intubation [18,20].

Talucci *et al.* [21] reported a similar experience at their institution. Over a 29-month period they committed 260 spontaneously breathing trauma patients to rapid sequence orotracheal intubation after administration of thiopentone and suxamethonium. There were no serious haemodynamic or neurological sequelae. Seven patients had a serious cervical spine injury. Cervical spine evaluation was not obtained before intubation, which was conducted with in-line traction. Unfortunately, the details of those aspects of management were not supplied.

Checkan and Weber [22] examined retrospectively the use/nonuse of muscle relaxants in 16 patients intubated for cervical spine injury. They found that in their institution patients who received muscle relaxation before intubation had significantly higher Glasgow coma scores, but neither group had any neurological complications following intubation.

Concerns over neurological assessment following induction of anaesthesia and orotracheal intubation have prompted some workers to use awake tracheal intubation. A retrospective study of this technique has been described by Meschino *et al.* [23]. Three of 136 patients with an acute cervical spine injury who required tracheal intubation (whether oral or nasal was not stated) suffered a deterioration in neurological status between initial examination and discharge. This was not significantly different from the deterioration rate (5 out of 233) of a second group of cervical spine injury patients in whom the trachea was not intubated. The possible advantages of awake intubation in a conscious, cooperative patient with a cervical spine injury is academic in respect of the ATLS protocol, which is concerned with the unconscious patient.

The studies quoted are all readily criticised because of difficulties in methodology or their retrospective nature. Despite these limitations, the oral route for tracheal intubation clearly has a good clinical track record and the objections to its use in cervical spine injury remain unproved.

Nasotracheal intubation

The use of nasotracheal intubation to control the airway of spontaneously breathing patients is a popular technique in American emergency rooms. Despite ATLS approval there is no evidence that this route of intubation is safer in spontaneously breathing patients with a cervical spine injury.

The effect of nasotracheal intubation on cervical spine movement has been inadequately investigated. Aprahamian *et al.* [15] found that blind nasotracheal intubation produced > 5 mm of posterior subluxation when the neck was stabilised anteriorly by hand pressure. This was reduced to 2 mm by omitting stabilisation but the effect of this on the ease of intubation was not mentioned.

Bivins *et al.* [14] did not use nasotracheal intubation but approved its use in trauma patients who require immediate intubation.

Holley *et al.* [24] reviewed retrospectively the airway management of 113 patients with unstable injuries which required operative fixation. The patients had either a partial or no neurological deficit. Nasal or oral intubation occurred in 86 (25 with neurological deficit) and 27 (8 with neurological deficit) patients respectively. Neither group had changes in neurological status. The authors concluded that both routes of intubation are acceptable in the operating theatre but cautioned against extrapolating their findings to the acute situation in the emergency room.

Success rates of over 90% have been reported for blind nasal intubation in emergency patients [25–27] but this is not invariable. Dronen *et al.* [28] compared blind nasal and oral intubation in a study of drug overdose patients. Oral intubation was found to be superior in terms of success rate (100% v 65%), time to accomplish (64 v 276S) and mean number of attempts (1.3 v 3.7). The blind nasal group had a complication rate of 86% (69% epistaxis, 17% vomiting, 10% aspiration). Multiple attempts at nasal intubation are not unusual [28].

These findings support many of the reservations about the advisability of nasotracheal intubation in patients with cervical spine injury. Coughing can be controlled with translaryngeal anaesthesia but this may increase the risk of aspiration [29]. Semiconscious or apparently comatose patients may still respond with other involuntary movements. Apnoea is an important contraindication and there are also objections to the use of the nasal route in the presence of a basal skull fracture [30].

'Light-wand' intubation

The light-wand is a flexible stilette which contains a distal light bulb, over which a tracheal tube can be fitted. When inserted blindly into the mouth the light serves to guide correct placement of the tracheal tube through the glottis. The technique is essentially a modification of the tactile method of tracheal intubation, which itself has been suggested to be beneficial in cases of cervical spine injury [31].

Fox *et al.* [32] compared blind nasal and light wand intubation in patients subjected to awake intubation before laminectomy. The light-wand resulted in significantly fewer intubation attempts, which were accomplished faster and with less complications. In their discussion the authors stated that this technique is used frequently in their institution for patients with cervical spine injury.

Ellis *et al.* [33] made a comparison between the light-wand and direct laryngoscopic techniques in elective surgical patients. Intubation at the first attempt was successful in 72% and 98% of the light-wand and direct groups respectively. Times for intubation did not differ, but patients in the light-wand group had a significantly lower incidence of movement, coughing or bucking. The relevance of this is difficult to assess as all patients were supposedly paralysed at the time of intubation.

While the Fox and Ellis studies were completed under controlled conditions, a report of field experience is available [34]. Twenty-four light-wand intubations were attempted in 21 patients with a success rate of 88%; direct laryngoscopy had failed in 10 patients. Of the three unsuccessful cases, all had vomited and two intubations were attempted in bright sunlight. Clinical details of the patients were not supplied.

A longer stilette has been used to facilitate nasotracheal light-wand intubation. Verdile *et al.* [35] compared its effectiveness with blind nasal intubation in a study of 80 apnoeic surgical patients. The light-wand enjoyed limited success; tracheal intubation was successful in 63% of patients compared to 41% in the blind nasal group. The times taken to intubate were not significantly different but there were wide variations in the success rates of different practitioners. The same observation has been noted for the oral route where success is influenced positively by training on cadavers [36].

All of these studies describe the need in some cases to manipulate either the jaw or larynx before insertion of the tracheal tube or stilette. There are no radiological studies of the effects of these techniques on the normal or injured cervical spine.

Clinical reports of the use of the oral technique in cervical spine injury remain limited [32,37]. One case report describes the use of the nasal stilette in a patient with maxillofacial trauma [38].

Fibreoptic tracheal intubation

The successful use of fibreoptic intubation to overcome intubation difficulties secondary to cervical spine pathology is well documented [39–41]. The technique is accomplished using topical or general anaesthesia, by either the oral or nasal route.

Successful fibreoptic intubation depends on proper training and sensible patient selection. Appropriate local anaesthesia is essential in the awake patient to prevent bucking or coughing. While fibreoptic intubation is possible in patients at risk of aspiration [42] there are other concerns in trauma patients. The technique requires time and may be impossible in the presence of extensive secretions, blood, vomit or anatomical distortion [43,44]. The procedure is technically easier in a sitting patient, but this may not be possible in cervical spine injury. Mlinek *et al.* [45] observed that these considerations limit its use in acute situations, although they listed proven or suspected cervical spine injury as an indication. The ATLS acknowledges a role for fibreoptic intubation but a lack of training and experience is liable to restrict its use in British practice.

The Bullard laryngoscope

The Bullard laryngoscope combines a rigid anatomically shaped blade with a fibreoptic light source. This combination affords an indirect view of the larynx. Tracheal intubation takes place using a guide-wire or forceps passed through a working channel of the laryngoscope. Alternatively, the tracheal tube is passed with the intubator's free hand while the larynx is viewed through the instrument's viewing piece.

The Bullard laryngoscope has been used successfully in both adult and paediatric patients with unstable cervical spine injury [46,47]. Visualisation of the glottis is usually easy but insertion of the tracheal tube may be difficult. Threading the tracheal tube over the guide wire may be the best approach [48].

The Laryngeal Mask Airway (LMA)

Calder *et al.* [49] described the use of the LMA in a patient who developed pulmonary oedema after transoral odontoidectomy and posterior occipitocervical fusion. Another report describes the use of a LMA during anaesthesia in an individual with an unstable cervical spine injury [50]. The LMA has been used to maintain an airway in other cases where tracheal intubation proved impossible, and the relative ease of insertion is likely to make its use in cervical spine pathology the subject of further investigation.

Retrograde intubation

Retrograde intubation involves the blind insertion of a tracheal tube into the trachea over a guide-wire or catheter passed retrogradely into the oropharynx through the cricothyroid membrane [51]. The effectiveness of the technique may be improved by passing the guide-wire through the 'Murphy eye' of the tracheal tube [52].

Retrograde intubation has been used successfully in trauma patients [53]. All of the 19 patients in this series suffered maxillofacial (12 patients) and/or cervical spine injury (7 patients). The trachea was intubated retrogradely at the first attempt in all patients (duration < 5min), including 13 in whom conventional oral/nasal intubation had failed. If a central venous pressure catheter was used as the intubating guide, the ability to inject air assisted location in the mouth in cases of severe facial haemorrhage. Despite restrictions on head and neck movement, puncture of the cricothyroid membrane was accomplished without difficulty; the only reported complication involved minor bleeding at the site in three patients.

Cricothyroidotomy

The ATLS has relaxed its original position and now teaches that an inability to intubate the trachea is the only indication for creating a surgical airway. Cricothyroidotomy includes: (1) surgical 'cut-down' on to the cricothyroid membrane with subsequent passage of a tracheal/tracheostomy tube of up to 8 mm external diameter. This procedure should not be attempted in patients under 12 years of age [6]: (2) Cricothyroid membrane puncture using a 12–16 gauge needle/catheter attached to a high pressure oxygen source (50 psi) or anaesthetic circuit.

A variety of equipment assemblies have been described that will permit oxygenation and ventilation [54–56]. Percutaneous tracheal puncture is possible as an alternative to cricothyroidotomy [57].

The effect of cricothyroidotomy on cervical spine movement has not been studied. A careful approach to identification of the anatomical landmarks of the neck is required to avoid misplacement of the airway. This can be difficult in obese or well-built patients and is normally made easier by active extension of the neck. The risk of misplacement is increased if a neutral neck position must be maintained.

The importance of restricting the use of surgical access to the airway in cervical spine injury is realised when the complications of cricothyroidotomy are examined. As a substitute for formal tracheostomy, elective cricothyroidotomy has a low overall complication rate and minimal long-term pathological sequelae [58–60]. This contrasts with a complication rate of 31% when cricothyroidotomy was performed for immediate airway control in the field [61]. Use of the technique in the emergency department is associated with an immediate complication rate of 32% [62]. However, these two studies contain only 10 patients with isolated cervical spine injury and airway compromise, and individual details of their outcomes are not supplied.

Conclusion

Rational management of the airway in patients with cervical spine injury is frustrated by the lack of prospective clinical studies comparing the outcome of different techniques. The difficulties of such research are obvious. The risk of precipitating neurological injury from airway manipulation in patients with cervical spine injury is unknown and may be more theoretical than practical [63]. The ATLS protocol is limited, not least in that it fails sufficiently to balance this consideration against the potential dangers of some of the prescribed airway manoeuvres. An attempt to select the method of airway management according to the 'degree of risk' has been made [64] but this assumes expertise with fibreoptic intubation. Possibly the most important consideration for the British clinician is to be aware of the traumatic injuries associated most commonly with cervical spine injury and subsequently to proceed with techniques with which he/she practised [65]. Continuing education to extend the range of airway skills is desirable and the benefits will not be confined to trauma care.

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Anaesthesia, 1992, Volume 47, pages 798–800

SPECIAL COMMUNICATION

Advanced trauma life support

A time for reappraisal

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Summary

The experience of Advanced Trauma Life Support training received by three anaesthetists is discussed with particular reference to the teaching of airway management, the grade of staff who should attend the present courses and the relevance to the British hospital system. We conclude that these courses are useful but limited by their inflexibility and failure to recognise the difference in skill mix in the British setting.

Key words

Anaesthesia; trauma.
Education.

Over half a million trauma victims are admitted to hospital in the UK each year [1]. Approximately 40 people per day, or 14 500 per year, die as a result of trauma. It is the leading cause of death in the under-35-year age group. Deaths from AIDS are rare in comparison, yet only a small percentage of resources are channelled into research and prevention of trauma.

The report of the Royal College of Surgeons of England [1] identified suboptimal management as a contributory factor in the high morbidity and mortality of trauma patients in hospital. One initiative has been the adoption of Advanced Trauma Life Support (ATLS) provider courses from America. ATLS started in the UK in 1988 with one course; this year there will be over 40 courses. This has led to the widespread introduction of ATLS teaching in accident and emergency departments.

We review our experiences of three different ATLS provider courses which we attended.

The origins of ATLS

The concept of ATLS arose from an accident in the deserts of Nebraska, USA, in 1978. A surgeon was piloting a light aircraft which crashed, killing his wife and injuring his three children. No emergency services had been alerted and he had great difficulty in getting his children and himself to the local hospital. On arrival he felt that the basic trauma care was inadequate. Following his experiences, he set up the ATLS courses, aimed at staff found in this type of isolated (community) hospital. However, ATLS is now being taught widely in the USA and is being introduced throughout the world as an exact, verbatim replica of the American course (apart from the use of animal models for teaching practical skills [2]).

The aims of ATLS

The aim is clearly described in the course as, the appropriate management of patients in the early period following trauma—the so-called 'Golden Hour'. Such management should not only reduce mortality at this time but also reduce the morbidity and mortality which occur in the period 10–21 days after trauma [3]. ATLS achieves this by concentrating on basic, safe management principles and teaching several practical skills. These skills assist not only in the management of the patient but also provide diagnostic information which should alert the isolated physician to the need for appropriate referral or assistance. To this end, ATLS achieves its aim well. It is a deficiency in our medical training that such basic skills and knowledge are not learnt by our junior doctors at an early stage in postgraduate training or even at medical school.

How does it work?

The 3-day course consists of lectures, practical instruction (skill stations) and the moulage (rôle play of a trauma situation). The content is strictly laid down by the

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American faculty. Each instructor may be called upon to teach any part of the course irrespective of that instructor's parent discipline. ATLS training uses algorithms for the trainee to follow. The algorithms concentrate on resuscitation and review until the patient is stable. Further algorithms are used to assess other injuries and lead the physician to decide on referral to a general, orthopaedic, cardiothoracic or neurosurgeon, either within the hospital or elsewhere. There may be situations in which stability cannot be achieved without surgical intervention, in which case the patient is likely to die if no surgeon is available.

The algorithms are based on the presence of a three-tier hospital system as exists in America, including the community hospital (level 3), the district hospital (level 2) and the regional hospital (level 1 Trauma Centre). Trauma services in the UK have been developed on a two-tier system—district general and teaching hospitals, both of which have all basic specialties.

Problems

The three authors, as anaesthetists, identified a number of potential problems in the ATLS teaching, and it is likely that other specialists may have disagreements with the teaching related to their own discipline. None of the algorithms led to a request for the services of an anaesthetist. It is argued that the isolated doctor has no time to send for an anaesthetist, and that a difficult airway problem must be managed to the best of his/her ATLS skills. This may be appropriate in America, but in the UK there are very few acute admitting hospitals which do not have an anaesthetist available within minutes, or present in the Emergency Department when the patient arrives. This is preferable to the anaesthetist being sent for after the ATLS-trained casualty officer and surgeon have spent time with the patient. In the smaller British hospitals, the most experienced resident doctor may often be the anaesthetist.

Anaesthetists are not mentioned anywhere in the course, and inspection of the course faculty in America reveals no anaesthetic input. Some trauma centres in America, such as Baltimore, advocate the use of anaesthetists specialised in trauma care to lead the trauma team [4], although this is against the ATLS faculty recommendations. Some courses in this country have no senior anaesthetist among the instructors.

Anaesthetists should be familiar with the doctrine of ATLS and will benefit from the practical experience of the other techniques taught. In addition, they posses other skills which may decrease morbidity in the less severely ill patient and which may be life-saving in the severely traumatised patient. ATLS training does not allow the use of drugs such as sedatives, analgesics and muscle relaxants to facilitate tracheal intubation. In the semiconscious patient, ATLS training advocates the use of blind nasal intubation, a technique not without hazards, rather than using drugs to aid tracheal intubation (Fig. 1).

Another feature in the management of patients is that central venous cannulation for resuscitation is discouraged on the basis that, in the hands of an inexperienced operator, the complications outweigh the benefits. This dogma fails to address the fact that such skills are often available and in many instances more appropriate than a surgical cut-down.

These criticisms do not imply that ATLS training is wrong. It is one system, but within that system consideration should be given to the specialist experience which is often available in British hospitals, otherwise senior medical staff will find the course less valuable and may not attend. Indeed, these skills may be used more appropriately in conjunction with the training offered by ATLS.

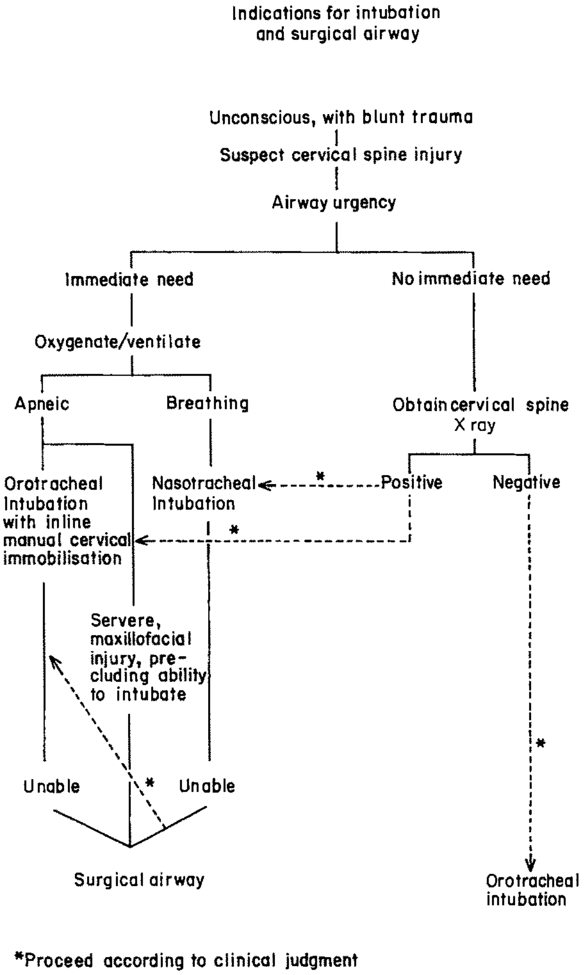
Indications for intubation and surgical airway
Unconscious, with blunt trauma
Suspect cervical spine injury
Airway urgency
Immediate need
No immediate need
Oxygenate/ventilate
Apneic
Breathing
Obtain cervical spine X ray
Orotracheal Intubation with inline manual cervical immobilisation
Nasotracheal Intubation
Positive
Negative
*
Servere, maxillofacial injury, precluding ability to intubate
Unable
Unable
Surgical airway
Orotracheal intubation
*Proceed according to clinical judgment

Fig. 1. Indications for intubation and surgical airway (reproduced by kind permission of the Trauma Committee of the American College of Surgeons).

To whom is the course directed?

The Royal College of Surgeons of England supports attendance by junior doctors at ATLS courses [1]. However, the ATLS Working Party anticipates that consultants and senior registrars, especially those who may be members of a Trauma Team, will be the main attenders. As there are potential advantages in having one system, the whole Trauma Team should benefit from ATLS. Specialists can learn from other disciplines; for example, many anaesthetists would benefit from the lessons on interpretation of cervical spine X rays, but it is naive to have an orthopaedic registrar teaching trained anaesthetists about the management of the paediatric airway or the reverse in the case of spinal injuries. Recognition of specialised skills needs to be incorporated into the course, otherwise it becomes a pantomime. Some ATLS courses do recognise the benefit of a specialist teaching within his/her specialty, although this is against one of the concepts of the course.

The relevance of ATLS training to British hospitals

During the course, much emphasis is placed on working through trauma scenarios on paper, and with people modelling as trauma patients, the so-called 'moulage'. In both cases, the common thread is that you are isolated in a hospital, usually 100 miles from a Trauma Centre, and with no surgical support immediately available. As noted above, anaesthetic availability is not mentioned, a situation which is unusual in the UK. The Royal College of Surgeons provided funds for a retrospective enquiry into 1000 cases of deaths due to trauma [1]. The results indicate that of 170 preventable deaths, 22 were due to hypoxia and 15 of these secondary to aspiration. This shows the need for skilled staff as early as possible in trauma cases and that aspiration, although not specifically mentioned in the ATLS course, is an important factor. It concludes that major trauma care should be regionalised and that every effort must be made to bring the patient to such a centre during the 'Golden Hour', where expert anaesthetic and surgical help must be at hand. It also recommends changes in postgraduate education to allow specialists to rotate through an Accident and Emergency Department.

The standard of trauma care could undoubtedly be improved in the UK, but should we propagate a course which was not designed for the British system? The ATLS handbook, containing the course material, is reviewed every 4 years and the next edition is to contain some suggestions from the British ATLS Working Party [2]. There will not be a separate British handbook and the different rôles of anaesthetists across the Atlantic are unlikely to be recognised.

The evidence that ATLS is effective

Irving [5] cites missed diagnoses, continuing haemorrhage, hypoxia and lack of timely surgery as the major reasons for poor outcome in trauma, but it has been shown that the establishment of trauma centres has improved outcome in both the UK and America [5,6]. Trauma scoring systems, such as the Revised Trauma Score, have proved useful to indicate when expert help should be requested [7].

One Accident and Emergency Department in Vancouver tried to quantify the improvement in patient outcome before and after the introduction of ATLS training [8]. The authors documented all trauma patients one year before and one year after the introduction of ATLS training and showed no difference over the 2-year period.

The ATLS Working Party in the UK is about to launch a questionnaire survey of those who have attended ATLS courses to establish if their practice has changed. They will also be attempting to assess whether outcome has been improved in departments which incorporate ATLS. Both studies will have implications regarding the future of ATLS in the UK.

ATLS is not a 'magic bullet' for tackling the enormous number of trauma victims admitted to hospital but improved training and outcome audit are to be welcomed in Accident and Emergency departments. ATLS courses may be an important adjunct to training, as suggested by the Royal College of Surgeons, but there is no evidence to date that this is so.

It is perhaps too harsh to describe ATLS as 'gimmicky' but it is a 'package deal'. If there is a place for algorithms in trauma then a recognition of specialist skills should be incorporated, otherwise they may result in inferior care and the ATLS courses will fail to attract senior medical staff.

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Forum

The pre-operative anaesthetic visit

Its value to the patient and the anaesthetist

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Summary

One hundred and thirty-two patients staying in hospital more than 24 h were visited pre- and postoperatively. Patients were asked a standard set of questions, and 39% could not remember accurately what they were asked. This has important medicolegal implications. In 15% of patients, information that significantly altered subsequent anaesthetic management was discovered, but in less than 3% would ignorance of the patient's condition have required postponement of the surgery. We conclude that the major reason for a pre-operative visit by an anaesthetist is that patients appreciate it, rather than it being medically necessary.

Key words

Anaesthesia; pre-operative visit.

The pre-operative visit by an anaesthetist is a controversial subject, of which even the primary purpose is debated [1]. As the workload of anaesthetists in the operating theatre increases, the time available for pre-operative visiting becomes more scarce [2], and inevitably, time spent outside the operating theatre by anaesthetists will become subject to scrutiny by management in search of ever more efficient working practices. Anaesthetists therefore need to ascertain more clearly the purposes and benefits of the pre-operative anaesthetic visit.

The aim of this study was to: assess the frequency with which information that significantly affected anaesthetic management was elicited at a pre-operative visit; obtain the patients' assessment of the value of the pre-operative visit; assess the accuracy of recall of specific questions asked at the visit bearing in mind the medicolegal importance of such questions.

Methods

One hundred and thirty-two patients scheduled to undergo elective surgery were included in the study; all were in-patients at Salisbury District Hospitals. Patients who were expected to be discharged during the first 24 h post-operatively or who were under 16 years of age were not studied. The surgical specialties included were general surgery, orthopaedic, gynaecological, ear, nose and throat, plastic and oral surgery.

Each patient was visited pre-operatively by whichever of the authors was scheduled to administer the anaesthetic. A standard verbal explanation of the forthcoming events was given, based on the Association of Anaesthetists' booklet *Your Anaesthetic* [3]. Patients were then asked a standard list of questions, including whether they were taking any medication and whether they had ever been jaundiced (Table 1), followed by any further questions that the anaesthetist considered relevant. A clinical examination was performed as appropriate. The anaesthetist recorded at this time whether he had elicited any information during the interview which would alter his peri-operative management of the patient.

An anaesthetic technique appropriate to the individual patient was adopted; no attempt was made at standardisation.

Patients were subsequently interviewed during the first postoperative day by one of the authors who had not been involved with the anaesthetic. We introduced ourselves as doctors conducting a survey, but did not mention that we were from the anaesthetic department. A standard list of

Table 1. Standardised pre-operative questions.

1. Have you had a previous anaesthetic? If so, was it within the last 3 months? Were there any problems?
2. Have you or any blood relatives suffered an unusual reaction to an anaesthetic?
3. Have you had: any serious illnesses?
   heart disease?
   chest disease?
4. Have you ever been jaundiced?
5. Do you normally take any medicines?
6. Are you allergic to any drugs?
7. Are there any questions that you would like to ask me about your anaesthetic?

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Table 2. Standardised postoperative questions.

		n = 119	
		Yes	No
1.	Were you seen before your operation by an anaesthetist?	112	7
		n = 112	
2.	If so, did he/she ask you		
	(a) whether you were currently taking any medications?	103	9
	(b) whether you had ever been jaundiced?	75	37
3.	How helpful did you find this visit? Would you rate it on a scale from 1 to 5, 1 being totally useless, and 5 very useful?		
	Score *No.* 1 3 2 0 3 11 4 29 5 69		
4.	Have you suffered any ill effects that you attribute to your anaesthetic?		

questions was again asked (Table 2). This included an enquiry as to whether the patient had been seen pre-operatively by an anaesthetist and if so, whether he/she had been asked if he normally took any medicines, and if he/she had ever been jaundiced. Patients were then asked to give their subjective opinions of the value to them of the pre-operative visit by rating it on a scale from 1 (no value) to 5 (very valuable).

Results

All one hundred and thirty-two patients were visited pre-operatively: 51 were male and 81 female. Their mean age was 51 years (range 16–99).

Factors which were judged to warrant a modification of the anaesthetist's usual peri-operative management were identified in 20 (15%) patients. A list of these factors is presented in Table 3; several factors were present in some patients.

In the authors' judgement, delaying surgery in order to instigate further treatment or investigation would have been necessary in three patients (2.3%) if the anaesthetist had not known of their condition, either from a pre-operative visit or by notification from the surgical team. The problems were: uncontrolled atrial fibrillation in one patient, untreated congestive cardiac failure in a second, and poorly controlled diabetes in the third.

Table 3. Factors affecting peri-operative management elicited at the pre-operative visit.

Significant abnormality of renal or hepatic function	3
Blind or deaf	3
Severe anxiety	3
Halothane anaesthetic within last 3 months	2
Request for regional anaesthesia	2
Severe COAD, requiring surgery to be performed under epidural anaesthesia	1
Severe opioid intolerance requiring regional analgesia postoperatively	1
Hyperparathyroidism and long-term steroid therapy	1
Insulin-dependent diabetes	1
Untreated hypertension	1
Uncontrolled atrial fibrillation	1
Postcricoid carcinoma, requiring rapid sequence induction	1
Previous head and neck surgery	1
Acute pulmonary tuberculosis	1
Epilepsy	1
Pregnancy	1
Severe obesity	1

COAD, Chronic obstructive airways disease.

One hundred and nineteen patients were interviewed postoperatively, the other 13 having been discharged earlier than anticipated.

Seven patients (5.9%) denied that they had been seen pre-operatively by an anaesthetist. Of these, one patient was a 99-year-old and could remember no peri-operative events. There was no obvious reason why the other six patients, whose mean age was 55 years, should have been unable to recall the visit.

Of the 112 patients who recalled a pre-operative visit nine (8%) denied being asked what drugs they were taking, 37 (33%) denied being asked about jaundice and 40 (36%) denied that one or other question had been asked.

If the 40 denying one or other are added to the seven denying a pre-operative visit, accurate recall of the pre-operative questions asked was deficient in 47 (39%) of the patients.

The patients' scores for the value of the postoperative visit are shown in Table 2. Ninety-eight patients (82%) gave a score of 4 or 5. Thus the majority of patients felt a pre-operative visit to be valuable.

Discussion

It is accepted as an integral part of the practice of high quality anaesthesia that patients are visited by the anaesthetist who will subsequently anaesthetise them; indeed such a practice is considered as a marker of quality.' It is therefore proper that we should know the reason for, and value of, such a visit.

The anaesthetist would seem to have four reasons for the visit: (1) to assess the patient's fitness for the surgical procedure proposed; (2) to discuss and decide upon the most appropriate anaesthetic technique; (3) to provide reassurance to the patient; (4) arguably, to prescribe premedicant drugs.

The Association of Anaesthetist mentions in its booklet *'Workload for Consultant Anaesthetists'* [4] the pre- and postoperative assessment of patients, implying that assessment is the principal purpose of the pre-operative visit. By contrast, the anaesthetic literature is almost exclusively concerned with the benefits to the psychological wellbeing of the patient. These have been found to include not only a reduction in anxiety [2, 5, 6] but also a decrease in postoperative analgesic requirements [7]. More extensive pre-operative preparation appears to confer other benefits, including an attenuated hormonal stress response and lower incidence of wound infection [8], better recall of the events on the day of operation, and earlier discharge from hospital [9].

In 15% of patients there was a complicating factor which the anaesthetist felt warranted an alteration of his usual peri-operative management. In all of these cases, prior notification to the anaesthetic department that pre-operative assessment was required would have sufficed, or if the surgical team was not aware of the significance of the finding, the anaesthetic technique could have been modified to accommodate the problem.

In less than 3% would failure to elicit potential problems prior to the patient's arrival in the anaesthetic room have required postponement of surgery. This is a lower figure than Holdcroft found from an anaesthetic assessment clinic [10], presumably because in the present study the inpatients had already been assessed by the surgical team before the anaesthetist visited them, although a few patients still slipped through the surgical screen.

Ninety-eight patients (82%) gave a value score for the pre-operative visit of 4 or 5. This suggests that the patients appreciate pre-operative contact with an anaesthetist, as well as benefit from a reduction in anxiety as a result of pre-operative psychological preparation for surgery [2, 5, 6].

The role of premedication is controversial. Whilst some patients undoubtedly suffer severe anxiety, often related to ignorance of what is to befall them, the benefits of routine pre-operative medication are questionable [11]. Anxiolytics can be prescribed by the house surgeon in accordance with agreed guidelines if necessary, although they are no substitute for adequate communication. We do not therefore consider the prescription of premedicant drugs to be an important purpose of the pre-operative visit.

The key questions are: (1) whether pre-operative rounds are cost effective; (2) whether pre-operative rounds are an essential element of quality anaesthesia.

A pre-operative round may take from 15 min to 1 h for a normal surgical operating list. It can be argued that a great deal of this time is often spent unconstructively chasing round different hospitals and wards finding patients when all are gathered in one place a little later for the list; but then neither is it constructive use of time to hold a list up to do an adequate assessment of the patient in the anaesthetic room. The balance between these two rests with the experience of the anaesthetist and the complexity of the list.

The quality issue is more difficult. We have shown that patients certainly appreciate the visit, but we have not attempted to ask whether the same cost, whatever it may be, would be more appreciated if spent in other ways.

The medicolegal consequences of inaccurate patient recall are interesting. Certainly accurate information about a patient is an essential prerequisite of anaesthesia; statements such as that from the Committee on Safety of Medicines [12] that 'A careful anaesthetic history should be taken to determine previous exposure ... to halothane' make careful pre-operative histories mandatory, and it may be that a hard-copy questionnaire has much to recommend it for medicolegal reasons. Neither our nor our patients' memories can be relied on!

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Chronic pain management training for senior registrars in anaesthesia

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Summary

In 1985 and 1990 postal questionnaires were sent to anaesthetic senior registrars in training in the United Kingdom to determine the extent of higher specialist training in chronic pain management. There were wide variations in training and experience amongst senior registrars. Overall there was little change between 1985 and 1990. In particular the number of anaesthetic senior registrars who felt equipped to undertake a consultant post with an interest in chronic pain management had not increased.

Key words

Pain; chronic pain management.
Education; higher specialist training.

The composition of both basic and higher specialist training programmes in anaesthesia is under continuous review. Subspecialties such as paediatric, obstetric and cardiac anaesthesia have an established place in training programmes, and the need for training in the management of acute pain control has been highlighted recently [1, 2]. However, the organisation of training in chronic pain management for senior registrars in anaesthesia has received less attention. In 1985 we conducted a postal survey of anaesthetic senior registrars in the UK requesting details of their training in the management of chronic pain. At that time many of the respondents stated that improvements were proposed. In 1990 we repeated this postal survey in order to assess the changes that had occurred in the intervening 5 years.

Methods

A questionnaire was sent to all senior registrars in anaesthesia in the UK. Their names and hospital addresses were sought from those involved in the organisation of higher specialist training programmes in each region, but senior registrars abroad and their locums were omitted from the survey. The questionnaire in 1990 was identical to that used in 1985 except for two questions which senior registrars were unable to answer accurately unless they had completed their training.

The 1990 questionnaire is shown in Figure 1. Each questionnaire was coded so that they could be identified by region for analysis but not by individual. A stamped addressed envelope was included. One reminder was sent if no reply had been received after 3 months.

Results

In 1985 questionnaires were sent to 407 senior registrars and 299 replies were received, a response rate of 73.5% (range of regional response rate 54.5% to 100%). In 1990 questionnaires were sent to 438 senior registrars and 310 replies were received, a response rate of 70.8% (range of regional response rate 52.6% to 100%).

Consultant sessions in chronic pain were almost universal in hospitals in which senior registrars were undergoing their training: 88% of senior registrars in 1985 worked in such departments and 89% in 1990 (question 1).

In 1985, 57% of senior registrars had a specific rotation for training in chronic pain management and this applied to 60% of the 1990 respondents. The regional variation is shown in Table 1. Within the group of senior registrars who had specific training rotations in chronic pain there was great variability in the length of time devoted to this, ranging from one session per week over as little as a month to 2 months spent exclusively in a pain unit. This was not only a difference between rotations in different regions but

Table 1. Positive answers as a percentage by region, giving total number of respondents in brackets, to Question 2(a) 'Does your senior registrar training scheme have a specific rotation in chronic pain management?'

	1985	1990
Aberdeen	0 (3)	75 (4)
Belfast	0 (15)	20 (15)
Birmingham	6 (16)	15 (20)
Bristol	94 (17)	65 (17)
Cambridge	60 (10)	91 (11)
Cardiff	31 (16)	42 (12)
Dundee	0 (2)	40 (5)
Edinburgh	50 (6)	9 (11)
Glasgow	0 (14)	100 (16)
Leeds	77 (13)	85 (14)
Leicester	89 (9)	100 (7)
Liverpool	95 (18)	75 (20)
London	65 (81)	59 (70)
Newcastle	100 (12)	88 (16)
Nottingham	70 (10)	86 (7)
Manchester	57 (21)	53 (17)
Oxford	100 (11)	100 (16)
Sheffield	20 (10)	70 (10)
Southampton	40 (15)	20 (15)
Army	—	63 (8)
Navy	—	0 (1)

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Training in chronic pain management: a questionnaire to Senior Registrars in Anaesthesia

	Yes	No
(1) Does your department have consultant sessions in chronic pain management?	☐	☐
(2) (a) Does your senior registrar scheme have a specific rotation for training in chronic pain management?	☐	☐
(b) If so, for how long?	________	
(3) If there is no specific pain rotation, how many pain sessions do you attend per year?	________	
(4) Does your Pain Clinic have an input from other specialists, e.g. psychiatrists, physiotherapists, acupuncturists, etc.? Please specify which specialists:	________ ________ ________ ________	
(5) Is there any research in chronic pain management underway in your department?	☐	☐
(6) Do you feel that you have, or will receive, adequate training in pain management to equip you to apply for a consultant post with a commitment to the treatment of chronic pain?	☐	☐

Please add any additional comments:

Fig. 1. The 1990 questionnaire.

there was considerable variation in the training received within some regions.

In 1985, 12% of all senior registrars who replied had no access to a specific chronic pain rotation and this figure had decreased to 9.5% in 1990. Some of these senior registrars had exposure on a sessional basis and the number of such sessions is illustrated in Figure 2.

Thirty different categories of other medical specialists, nurses, paramedical specialists and alternative medical practitioners were involved in the pain clinics attended by the respondents (Table 2). In 1985, 86% of respondents stated that their clinics had input from some other specialists; this had decreased to 68% in the 1990 survey.

In 1985, 45% of senior registrars were aware of some research in chronic pain management in their department and this figure had increased to 59% by 1990.

There was great variability both amongst different regions and little consistency within regions over the intervening 5 years in response to question 6—whether senior registrars felt that they would have had adequate training to take up a consultant post with a commitment to the treatment of chronic pain. Table 3 illustrates this wide variation. There was no clear link between the provision of a specific rotation and senior registrars' confidence in the adequacy of their training. Overall, 39% of respondents in 1985 and 37% in 1990 felt that their training equipped them to apply for such consultant posts.

Table 2. Other specialists (%) involved in the pain clinics attended by the respondents.

Specialty	1985	1990
Acupuncture	19	14
Physiotherapy	46	28
Psychiatry	44	19
Psychologist	40	24
Surgical specialties	50	31
Medical specialties	41	27
Alternative	3	5
General practitioners	3	1
Paramedical	13	14

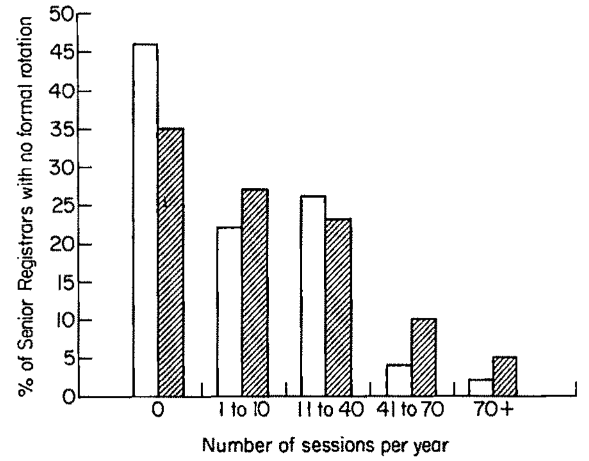

Fig. 2. Percentage of senior registrars replying to the questionnaire with no formal rotation in chronic pain management and the number of chronic pain management sessions they attended per year (□, 1985; ▨, 1990).

Discussion

The number of questionnaires sent to senior registrars in 1985 and 1990 was comparable, with a similar response rate. This, however, varied from region to region, which may reflect the difficulty in tracing some senior registrars who moved hospitals frequently during their training. There may also be a bias: those whose training was either particularly good or particularly bad might be more likely to reply. Overall, senior registrars worked in departments with similar access to consultant sessions in chronic pain management in 1985 and 1990 (88% and 89% respectively). There was a slight increase in those who have formal rotations in chronic pain, from 57% in 1985 to 60%

Table 3. The percentage of senior registrars replying that they felt competent to apply for a post with a commitment to chronic pain management (Question 6). The total number of respondents for each region is given in brackets.

	1985	1990
Aberdeen	33 (3)	25 (4)
Belfast	7 (15)	27 (15)
Birmingham	19 (16)	15 (20)
Bristol	59 (17)	24 (17)
Cambridge	50 (10)	18 (11)
Cardiff	6 (16)	33 (12)
Dundee	100 (2)	60 (5)
Edinburgh	33 (6)	0 (11)
Glasgow	21 (14)	31 (16)
Leeds	61 (13)	54 (14)
Leicester	33 (9)	71 (7)
Liverpool	72 (18)	65 (20)
London	41 (81)	49 (70)
Newcastle	71 (12)	50 (16)
Nottingham	60 (10)	14 (7)
Manchester	24 (21)	35 (17)
Oxford	73 (11)	75 (16)
Sheffield	10 (10)	50 (10)
Southampton	53 (15)	33 (15)
Army	—	37 (8)
Navy	—	100 (1)

in 1990. Some regions had obviously introduced rotations in the period between the surveys (Table 1), although the overall difference was small.

There continues to be a large variation in what constitutes a rotation, from one session per week for a month to 2 months full time commitment in a pain unit. As shown in Figure 2, many of the trainees who did not have a specific rotation nevertheless had significant exposure to chronic pain management. This often reflected the personal interest of the senior registrar rather than a planned training element. There was a slight increase from 14% to 18% in those who had or expected no exposure to chronic pain management training, but there was a marked decrease in those who recorded other specialist input into the Pain Clinic of their hospital from 1985 to 1990. This may reflect restrictions on the employment of paramedical staff, although there was also a marked fall in input from other medical disciplines. An aspect may be a shift towards anaesthetist-dominated Pain Services with a recognised sessional commitment.

Of note was the increased awareness of research activity within the chronic pain field. This may reflect development of pain clinics, which are becoming more established and thus have time for research as well as service, or simply an increased need for senior registrars to participate in research.

There was no great difference over the 5-year period in the number of senior registrars who felt that they would have had adequate training to embark on a consultant career with a commitment to chronic pain management, although there are an increasing number of consultant posts advertised with subspecialty interest in chronic pain management. It may be that senior registrars are not being adequately trained to meet these needs. Many senior registrars noted, however, that it could be 'arranged' to have more exposure to chronic pain management if they were particularly interested. A development has been a post-accreditation module which is already established in Manchester. Other regions are hoping to establish similar schemes in order to offer substantial training periods to those interested in the subspecialty.

Overall, little has changed since 1985 in senior registrar training in chronic pain management. With current interest in acute pain management [3, 4] and deficiencies in acute pain relief provision highlighted in the Report of the Working Party on Pain after Surgery [1] it is perhaps time to integrate training in the management of pain, both acute and chronic. It is difficult to accommodate all subspecialties in the higher specialist training programme, but we feel that senior registrars should at least have sufficient organised exposure to chronic pain management to allow them to decide whether they wish to pursue their interest further. Postaccreditation rotations would be preferable to the somewhat haphazard individual arrangements which exist in many regions. We feel that training in pain management in general is as important and relevant as training in other anaesthetic subspecialties. The alleviation of pain, acute or chronic, is a major part of the daily remit of anaesthetists and as such merits due emphasis in their training.

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A national database on hepatitis following exposure to inhaled anaesthetics

There is now compelling evidence that severe hepatitis following exposure to an inhaled anaesthetic is an immune-mediated phenomenon to a metabolite of the anaesthetic. Halothane is metabolised to the greatest degree, about 20% of an inhaled dose, and thus is the cause of the majority of cases of hepatic failure—so called 'halothane hepatitis'. This condition carries a significant mortality and may be an indication for liver transplantation.

We anticipate that in the near future we will be able to elucidate genetic factors which distinguish susceptible

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individuals. All halothane-exposed individuals metabolise halothane to trifluoroacetyl(TFA)-halide and thereby produce TFA-labelled proteins. The TFA-labelled proteins contain novel TFA-induced structural features (epitopes) which are not present on the unlabelled proteins. In the normal individual an immune response to the TFA-induced epitopes does not occur. However, in susceptible individuals, an immune response ensues and we believe that this is due to abnormal antigen presentation or immune responsiveness.

In order that we may pursue this hypothesis and identify molecular susceptibility factors, we wish to institute a Natonal Database of patients who have had severe hepatitis following exposure to an inhaled anaesthetic. We request that any practitioner having knowledge of such patients, past and present, contact us at St Mary's Hospital (letter or telephone call; 071 725 1681, direct line).

Antibodies to TFA-modified liver proteins are detectable in about 70% of patients with severe hepatitis and are specific to such patients. Their presence is therefore of diagnostic value and we offer an antibody testing service to any practitioner whose patient has severe, unexplained hepatitis following exposure to a volatile anaesthetic. Although halothane is the most common cause of hepatitis, other anaesthetics are metabolised to TFA to some extent and there exists the possibility that patients may become cross-sensitised to inhaled anaesthetics. We therefore wish to compile information and serum samples from all patients with unexplained hepatitis following exposure to any inhaled anaesthetic.

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Oxygen dynamics: more science at the bedside

Shoemaker and his colleagues [1] have demonstrated the importance of a supranormal level of oxygen delivery as at the very least a marker for improved survival in the critically ill, but the physiological terms involved in this context are perhaps still not widely used in the bedside language of intensive care, despite their current and future clinical implications. Some of these terms currently have several symbols to identify them, others have yet to gain them and perhaps it is time for standardisation. They include oxygen demand, oxygen debt, oxygen delivery (oxygen transport; current symbols include TO_2,$\dot{Q}O_2$ and DO_2), oxygen consumption ($\dot{V}O_2$), oxygen extraction ratio (O_2ER) and oxygen balance (the qualifications of 'positive' oxygen and 'negative' oxygen balance (hypoxia) might be useful here). A lack of appropriate monitoring equipment should not prevent our using these physiological concepts.

With advances in monitoring and with the possible exception of oxygen demand, we may well be able to assess regional as well as the less informative global changes in these parameters some time in the future [2]. Other concepts including physiological, and, for the moment, pathological oxygen supply dependancy are also important. We should now draw a clear distinction between 'hypoxia' and 'hypoxaemia', and if we are to be precise, between 'hypoxia' and 'ischaemia'. The blinkered oxygen therapy/mechanical ventilation approach to acute lung failure is belatedly changing to a more comprehensive cardiorespiratory approach towards the problem of oxygen balance. The adoption of these concepts should promote this advance which has been enhanced by recent work [3]. Recent studies on muscle fatigue have emphasised the clinical importance of distinguishing between respiratory work and respiratory function.

Finally, in view of the shape of the oxyhaemoglobin dissociation curve it is time we assigned oxygen saturation a much greater practical importance than oxygen tension. 'We put him on a ventilator with PEEP because he was hypoxic' is no longer an adequate statement. Hypoxic or simply hypoxaemic (*P*ao$_2$ 8 kPa) or neither perhaps? Was there also clinical evidence of increased oxygen demand, e.g. an obvious increase in respiratory work, sepsis? What had PEEP to offer in terms of increased oxygen delivery and improved oxygen balance, where these changes are required, rather than simply a change in *P*ao$_2$ [4] . . .?

Incidentally, one manufacturer of a blood gas machine claims that it gives 'a Deep Picture' of oxygenation including 'total information on oxygen uptake, transport and release to the tissues' from the analysis of 85 μl of blood! 'Deep Picture' is perhaps a new scientific term since I have not met it before, but to suggest cardiac output, oxygen extraction and regional oxygen consumption ('total information') can be measured from one small quantity of blood is simply astonishing, although it comes from a highly reputable and respected company.

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Footnote

These abbreviations and symbols used in *Anaesthesia* are those published by the Royal Society of Medicine in *Units, symbols and abbreviations, a guide for biological and medical editors and authors.*

Problems of thermodilution cardiac output measurements in small patients

We have recently encountered problems during cardiac output measurements by thermodilution in small patients receiving infusions through the side arm of a pulmonary artery (PA) catheter introducer sheath.

In the first patient (53 kg), the syringe pump occlusion alarm sounded immediately following each injectate administration whilst the patient was receiving sedation through the side arm of the PA catheter introducer sheath

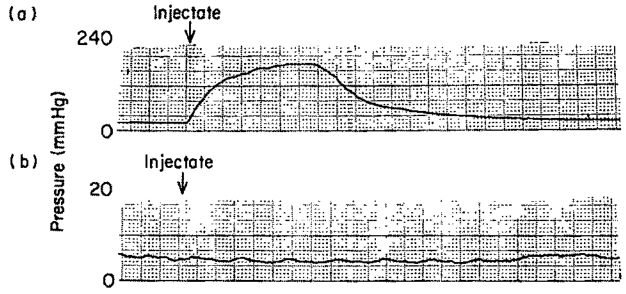

Fig. 1. Pressure tracings from the introducer sheath during cardiac output measurements in (a) a small patient (52 kg) when the injectate port lay within the introducer sheath and (b) a control patient (85 kg).

(7.5 F PA catheter). The second patient (weight 52 kg, height 158 cm), receiving inotropes through the introducer side arm, developed acute hypertension (from 120/70 mmHg to 230/120 mmHg) and briefly sinus tachycardia immediately following each injectate administration (7.5 F PA catheter). We initially hypothesied that there was a leak in the injectate channel proximal to the right atrial port. The inotropes were transferred to another route and the side arm of the introducer attached to a pressure transducer and paper recorder. A record was thus obtained of the pressure in the side arm during cardiac output measurements. Figure 1(a) illustrates the high pressures generated in the side arm during a very slow injectate administration in this patient and Figure 1(b) illustrates the pressures from a control subject (weight 85 kg, height 182 cm).

There was no defect in the PA catheter when removed and examined. However, it became clear that since the proximal central venous pressure (CVP) channel was 30 cm from the tip and only 43 cm of PA catheter lay in the patient, the proximal port must lie well within the introducer sheath (Fig. 2). Thus each injectate administration was delivered to the introducer interior, producing an acute rise in pressure, triggering the occlusion alarm in patient 1, and causing a bolus of inotropic agents to be delivered to patient 2 from the 'deadspace' of the introducer. Furthermore, since some of the injectate would remain in the introducer 'deadspace', there would be a small error tending to overestimate the true cardiac output.

Hannallah and White [1] reported a similar problem of erroneously high CVP measurements with the CVP port within the introducer sheath due to infusions through the side arm. This was not apparent in our patients. Most 7 F and 7.5 F PA catheters have injectate and infusion ports at 30–31 cm from the tip. A paediatric 5 F catheter has an injectate port at 15 cm and a PA catheter with a port at 25 cm is manufactured by Kimmal. Finally, the right ventricular port at 19 cm in an American Edwards Paceport catheter has been shown to give accurate cardiac output measurements [2]. As a consequence of this observation we now take greater note of the length of the PA catheter in the patient and are more circumspect in the choice of channel for inotrope administration.

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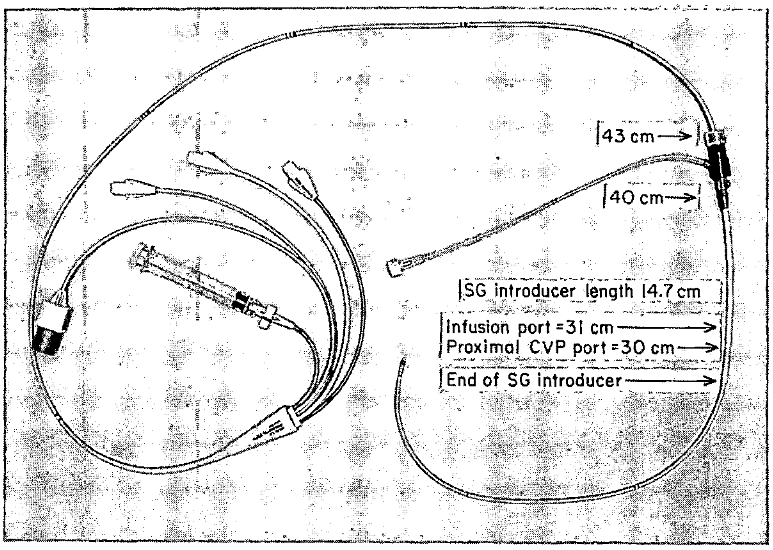

Fig. 2. Pulmonary artery catheter inserted through an introducer sheath indicating the CVP and infusion ports lying within the introducer sheath.

Pneumothorax and insertion of interpleural catheters

I have been reading with interest the techniques used for insertion of interpleural catheters. There are a number of complications associated with this technique [1], and pneumothorax is perceived to be the main problem, but this should not be the case, as already mentioned by Dobson and Peacock (*Anaesthesia* 1992; **47:** 272). Those anaesthetists who practice interpleural analgesia must make all attempts to minimise complications so that the technique is regarded as safe. More patients will then benefit from the superb analgesia offered.

I have been using the Arrow interpleural sets. These consist of a 17 gauge Touhy needle, a catheter, a filter and a one-way haemostasis valve. The interpleural space is identified using saline. The Touhy needle and attached haemostatic valve are connected to a 500 ml bag of normal saline and an infusion set with the valve open. As the patient breathes spontaneously at the end of operation, the Touhy needle is advanced over the superior aspect of the chosen rib with each inspiration. Identification of the interpleural space is distinct when the normal saline suddenly flows freely. The infusion is then stopped and the catheter passed through the one-way haemostatic valve. At no time during identification of the interpleural space or insertion of the catheter is air permitted entry to the interpleural space. This technique is safe, easy to learn, use and teach. It minimises the chance of pneumothorax. It also minimises the chance of misplaced catheters which have been reported [2], with associated failure of analgesia.

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Neurological sequelae in children after prolonged propofol infusion

The report by Trotter and Serpell (*Anaesthesia* 1992; **47:** 340–2) is of great interest as we recently encountered neurological signs in a child with croup who required prolonged sedation and was exposed to halothane, morphine, midazolam and propofol among other things. We do not feel confident, however, in solely ascribing the side effects seen to a propofol withdrawal syndrome.

A previously healthy, vigourous, 23-month-old, 15-kg boy was admitted with stridor due to laryngo-tracheo-bronchitis. His trachea was intubated during anaesthesia with halothane. He was then sedated with morphine and midazolam infusions; vecuronium was added to facilitate ventilation on days 2 to 5 (Fig. 1). When the latter was stopped, high dose midazolam was supplemented with trichloral syrup. A trial of extubation on day 6 was unsuccessful due to marked restlessness and stridor. Dystonic movements noted at that stage were attributed to midazolam, so he was then sedated with morphine infusion and trichloral. When this combination proved inadequate, propofol was commenced with good initial results. The propofol infusion rate was increased stepwise to 10.9 $mg.kg^{-1}.h^{-1}$ over the next 5 days. Fluid overload, hepatomegaly, a rise in liver enzymes (aspartate transaminase 244 $u.l^{-1}$, alkaline phosphatase 107 $u.l^{-1}$) and lipaemic blood on days 12–16, led to his sedation being changed to morphine, midazolam and vecuronium. Although all sedation was stopped on day 17, his trachea was not successfully extubated until day 21, mainly because of poor gas exchange.

Restlessness, which had been a feature throughout his illness, was associated with jerky, twitchy movements of the limbs, and functional blindness from days 17 to 33. An ophthalmologist who saw him on day 28 noted that he rubbed his eyes frequently, disliked light, and did not fixate or follow objects. He concluded that as ophthalmoscopy, electroretinograms and visual evoked potentials were all normal, the problem was one of attention defect and visual association. Motor function improved progressively over the next 2 weeks, while vision gradually returned to normal by day 33.

We considered metabolic disorders, encephalopathies and drug withdrawal syndromes. Viral studies, an extensive metabolic screen, electroencephalogram and computerised tomography of the brain were unhelpful. We felt that either midazolam or propofol were the most likely drugs to be implicated in a withdrawal syndrome, but unfortunately no drug levels were measured. However, it is worth noting that midazolam, like propofol [1] can accumulate especially in the presence of erythromycin (which this patient received), hepatic dysfunction and slow metabolism [2]. A withdrawal syndrome comprising confusion, irritability, visual hallucinations and fits has previously been linked with midazolam [3].

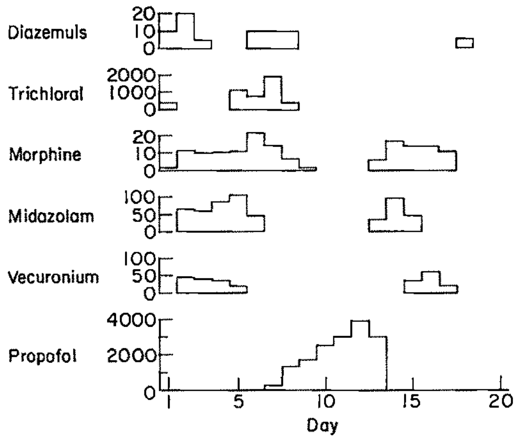

Fig. 1. Total daily drug dosages (mg).

No data on drug dosage is included in either of the 'propofol withdrawal' cases cited by Trotter and Serpell. Propofol has been associated with neurological side effects [4–9], while transient 'blindness' due to ptosis was recently reported in a 4-year-old boy who received midazolam, fentanyl and propofol [8]. Neither we, nor the manufacturers of midazolam and propofol, nor the Committee on Safety of Medicines (to whom this case has been reported) are aware of any previous reports of persistent functional blindness following propofol/midazolam infusion.

We accept that propofol does not have a product licence for intensive care sedation of children; the manufacturers do not support the use of propofol in young children for this purpose [9]. They have been notified of an unstated number of adverse neurological reactions, mainly occurring in young children with viral illnesses who received high dose propofol without opioids for sedation [9].

By contrast, low dose propfol infusion (say < 5 $mg.kg^{-1}.h^{-1}$) combined with an opioid infusion, has been widely and successfully used for short term sedation in children following surgery by us and others. The key difference seems to be the viral illness. It is possible that an unusually virulent virus is causing both a laryngo-tracheo-bronchitis and an encephalitis, or perhaps propofol/midazolam/other drugs are interacting with the viral illness to uncover neurological side effects. We therefore continue to support the careful use of low dose propofol combined with opioids for short term sedation of children on intensive care units following surgery, but on the evidence currently available, we suggest that propofol should not be used for sedation of children with viral illnesses.

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Propofol sedation of children

The report of neurological sequelae following prolonged propofol infusion in children by Trotter and Serpell (*Anaesthesia* 1992; **47:** 340), is a timely reminder of the difficulties faced by those charged with the sedation of children in intensive care. None of the agents commonly used in adult intensive care, such as midazolam, propofol, fentanyl, alfentanil, are licensed for long-term infusion in children [1]. There is, however, a clincial requirement for continuous intravenous sedation in paediatric intensive care, i.e. unlicensed drug use *must* occur.

The infusion rates used by Trotter and Serpell exceed those recommended for sedation of adult patients with propofol (Diprivan data sheet, ICI, 1992). These propofol infusion rates also considerably exceed those we have employed over the last 4 years for sedation of children following cardiac surgery. We studied a group of 20 of these children (median age 3.3 years). All received morphine by continuous infusion at 20 μg.kg^{-1}.h^{-1} in addition to propofol, but all but one child were adequately sedated at propofol infusion rates of $\leq$ 6.0 mg.kg^{-1}.h^{-1}. The median infusion rate after 24 h of propofol infusion was 2.70 mg.kg^{-1}.h^{-1}. There were no neurological sequelae in our patients. Perhaps the neurological sequelae in the patients reported by Trotter and Serpell were in some way related to the very high infusion rates used.

Neurological sequelae have been associated with a variety of sedative regimens in paediatric intensive care. A recent issue of the *Journal of Pediatrics* contained two reports of reversible neurological sequelae associated with various benzodiazepine–opioid combinations [2,3]. In an accompanying editorial [4], Kauffman alerts readers to the danger of children becoming 'therapeutic orphans' through lack of appropriate clinical trials. Kauffman comments that the risks inherent in administering a new medication in the context of a rigorously controlled clinical trial are far less than those inherent in the widespread exposure of children to therapies for which there is inadequate safety and efficacy information. We believe the report of Trotter and Serpell confirms this view. There is an urgent need for properly conducted clinical trials of propofol, and indeed other sedatives, used in paediatric intensive care. If such studies are not performed, there is a very real danger of potentially useful drugs, such as propofol, being condemned through heresay and problems reported during uncontrolled use. This is particularly important given a number of recent reports of significant problems noted during the management of children with laryngotracheobronchitis which included administration of propofol.

We believe it is important to prevent the further extension of the 'therapeutic orphan' status of critically ill children. Limiting use of 'new' agents to properly monitored clinical trials is one means of achieving this. Pharmaceutical companies have a responsibility to support such studies even if the market within the area is limited.

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Hoarseness after tracheal intubation

I read with great interest, and no little concern, the paper by M.W. Jones and colleagues (*Anaesthesia* 1992; **47:** 213–6). It is certainly alarming to note that from a total of 167 intubated patients five had suffered from postoperative hoarseness, which had lasted for more than a week and that in one of these the condition had persisted for 99 days!

For the investigation, a series consisting of 167 intubated patients must be regarded as quite small when considering the fact that the anaesthetic techniques were in no way standardised. Considerable space is given to describing the statistical methods used to try to evaluate the data but, strangely, no detailed information is given concerning the actual five cases with prolonged hoarseness. Would it be possible, perhaps, for the authors of the paper to supply us with this missing information? Above all it would be important to know the sex of the patient, the size of the tracheal tube used, and the duration of the anaesthesia in each of the cases with prolonged hoarseness.

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A reply

We are pleased that Dr Davies found our paper interesting. The idea for this prospective research came after reading a report of permanent hoarseness in 3% of women undergoing mastectomy [1], a figure we thought was truly alarming. We disagree with Dr Davies that our figures are alarming as none of our patients had permanent hoarseness. Of the 32% of intubated patients who were hoarse, 97% were normal at the end of a week and 98.8% were normal at the end of 2 weeks. Only two patients (1.2%) had significant problems which took 54 and 99 days to clear up. We will gladly supply Dr Davies with details on the five patients who were hoarse for longer than one week.

Patient 1 Hoarse for 9 days. Female aged 34 years weighing 62 kg given an anticholinergic with the premedication; anaesthesia was induced with thiopentone 425 mg followed by gallamine 160 mg. The cords were not sprayed with local anaesthetic prior to an easy intubation by a senior house officer with a size 8 mm red rubber tube without an introducer and the cords were seen to be wide open. KY jelly was used as a lubricant. Anaesthesia lasted 75 min.

Patient 2 Hoarse for 10 days. Male aged 51 years, weighing 78 kg not given a drying agent with the premedication; anaesthesia was induced with thiopentone 350 mg followed by pancuronium 8 mg. The cords were not sprayed with local anaesthetic prior to an easy intubation by a senior registrar with a size 9 mm Mallinkrodt tube with an introducer and the cords were seen to be wide open. KY jelly was used as a lubricant. Anaesthesia lasted 285 min.

Patient 3 Hoarse for 12 days. Female aged 73 years, weighing 45 kg given a drying agent with the premedication; anaesthesia was induced with thiopentone 50 mg followed by suxamethonium 100 mg. The cords were not sprayed with local anaesthetic prior to an easy intubation by a registrar with a size 8 mm Portex tube without an introducer and the cords were seen to be wide open. KY jelly was used as a lubricant. Anaesthesia lasted 80 min.

Patient 4 Hoarse for 54 days. Female aged 62 years, weighing 80 kg, not given a pharyngeal drying agent with the premedication; anaesthesia was induced with thiopentone 175 mg followed by suxamethonium 100 mg. The cords were not sprayed with local anaesthetic prior to a difficult intubation by a senior house officer with a size 8 red rubber tube with an introducer. The cords were seen to be moving during intubation. No lubricant was used. Anaesthesia lasted 10 min.

Patient 5 Hoarse for 99 days. Female aged 50 years, weighing 73 kg given a drying agent with the premedication; anaesthesia was induced with etomidate 18 mg followed by atracurium 40 mg. The cords were not sprayed with local anaesthetic prior to an easy intubation by a senior registrar with a size 9 mm armoured latex tube with an introducer and the cords were seen to be wide open. KY jelly was used as a lubricant. Anaesthesia lasted 15 min.

While the perusal of such raw data is interesting, no conclusions can be drawn from it without statistical analysis. In giving 'considerable space to describing the statistical methods' we sought to present valid conclusions from the data. In answer therefore to Dr Davies' specific points, the statistical methods used show clearly that the sex of the patient and size of tracheal tube were *not* significant in causing hoarseness, whereas duration of anaesthesia was significant. This is not apparent from the raw data on the fifth patient with prolonged hoarseness.

Finally we would point out that the anaesthetic techniques were 'in no way standardised' because, as stated in the article, the 235 patients were consecutive cases in the everyday workload of a District General Hospital. The usual practices of our anaesthetists were the subject of investigation.

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Reference

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Fibreoptic intubation under general anaesthesia need not be associated with hypoxia and hypotension

We read with great concern the article on oxygen saturation and cardiovascular changes during fibreoptic intubation under general anaesthesia by Smith *et al.* (*Anaesthesia* 1992; **47:** 158–61). The authors themselves state that the technique is not ideal, a rather euphemistic conclusion in view of a 30% incidence of $Sp_{O_2} < 90\%$ and an 8% incidence of $Sp_{O_2} < 80\%$. In one patient, a desaturation to 18% was triggered by an airway insertion. There are three aspects of this study that make the technique that was utilised problematical. Firstly, although none of their patients had normal airway anatomy, the authors were apparently confident that they would be able to maintain airway control after the induction of anaesthesia. Secondly, by not pre-oxygenating their patients and maintaining them after induction on 50% nitrous oxide in oxygen, they waived maximal oxygen reserve as required in patients with abnormal airways, for no obvious reasons. Thirdly, spontaneous ventilation with halothane caused severe cardiovascular depression necessitating the administration of haemaccel and atropine. The end-tidal CO_2 values and incidence of arrhythmia were, unfortunately, not provided.

The authors' conclusion that a technique involving muscle relaxants [1] might have been a better option for fibreoptic intubation in anaesthetised patients is supported by our findings. We used a fibrescope to intubate the tracheas of 50 consecutive patients (Cormack/Lehane Grade I and II) who were to undergo elective ENT surgery. All patients were premedicated with midazolam 7.5 mg and, after arrival in the operating theatre, intravenous access and appropriate monitoring were established. Anaesthesia was induced with fentanyl 0.2 mg followed by propofol 1 $mg.kg^{-1}$ as a bolus and a simultaneous continuous infusion fo propofol 10 $mg.kg^{-1}.h^{-1}$ reduced in 10 min intervals to a maintenance infusion of 60 $mg.kg^{-1}.h^{-1}$ [2]. When manual ventilation of the lungs with 100% oxygen was assured, 0.5 $mg.kg^{-1}$ atracurium was injected. As soon as a visible reaction to the train-of-

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four stimulation ceased, fibreoptic oral intubation was begun. Forty-five patients were intubated on the first attempt. The mean intubation time was 64 s (range 30–180 s). In five patients, multiple attempts were required for positioning the tube due to problems in visualising the larynx, secretions or problems in passing the tube through the laryngeal structures. Intubation time for these patients was between 5 and 11 min. Minimal Spo_2 and maximal CO_2 for all 50 patients were 96% and 5.3 kPa respectively. Systolic and diastolic blood pressures and heart rate, recorded at 1 min intervals during and 5 min following intubation, remained within 20% of control values, irrespective of the time required for a successful intubation. We did not use fibreoptic intubation aids; the jaw pull proved sufficient to open the retropharyngeal space.

Because of these results, we recommend total intravenous anaesthesia and complete muscle relaxation for fibreoptic intubation in patients in whom control of the airway is not a problem. Using this technique, dangerous desaturations and significant decreases in blood pressure can be avoided. When there is the slightest doubt regarding airway control after loss of consciousness, awake fibreoptic intubation is mandatory.

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A reply

It is unrealistic of Dr Schaefer and his colleagues to say that awake intubation is mandatory if there is the slightest risk of difficulty with the airway. What do they do with paediatric, confused or unconscious patients? We agree that awake fibreoptic intubation is ideal, but there is a need for a technique suitable for those patients that cannot tolerate an awake procedure.

Our study showed that fibreoptic nasotracheal intubation whilst the patient breathes halothane spontaneously was associated with hypoxaemia and hypotension. We used halothane with spontaneous respiration because this is often recommended for difficult airway problems, such as epiglottitis. So in answer to the first point, we were confident that we would be able to maintain an airway. To the second point we would agree that pre-oxygenation might have reduced the incidence of desaturation. We used 50% nitrous oxide in oxygen because we had found that it was difficult to keep the patients asleep without it, due to leaks. We found it interesting that cardiovascular depression was a problem at the same time that we were having difficulty maintaining a sufficient depth of anaesthesia. We do not have end-tidal CO_2 figures and there were no serious arrythmias, though extrasystoles were common.

Drs Schaefer, Marsch and Staender describe their experience with oral fibreoptic intubation in 50 normal patients, using an apnoeic technique. We presume these include the 30 patients they described elsewhere [1]. Intubation took less than a minute in those patients, but was prolonged (5–11 min) in five of their subsequent 20 (normal) patients. Marian *et al.* [2] found that Spo_2 declined rapidly after one minute of apnoea, despite pre-oxygenation. Since Schaefer *et al.* report that Spo_2 and $FE'co_2$ did not fall or rise, we assume that mask ventilation was applied from time to time. An apnoeic technique is satisfactory when the anatomy is normal and the operator experienced, but our paper addressed the problem of abnormal patients and many of the intubations were performed by trainees.

We now ventilate the lungs of our patients undergoing nasotracheal fibreoptic intubation under general anaesthesia through an oral airway. We use propofol for induction and maintanance and obtain paralysis with atracurium. For oral fibreoptic intubation under general anaesthesia, we use a method slightly modified from that suggested to us by Dr Fuge of Bath. Induction and maintenance is performed with propofol and alfentanil, mixed in the same syringe. Supplementary nasal oxygen is given and topical anaestheisa applied with 4% lignocaine in a spray as you go fashion. This works very nicely, but desaturation is more common than when ventilation is controlled.

In conclusion, we are indebted to Drs Schaefer and Marsch for their suggestion of total intravenous anaesthesia for fiberoptic intubation [1], which we have used, as described above, ever since. However, we feel that the apnoeic nature of their technique makes it unsuitable both for difficult patients who cannot tolerate an awake procedure and also, to a large extent, for training purposes.

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I read with interest the paper by Smith and colleagues concerning oxygen saturation and cardiovascular changes during fibreoptic intubation under general anaesthesia (*Anaesthesia* 1992; **47:** 158–61). However, this report requires some comment.

I was surprised to notice that 'the lungs were not pre-oxygenated' before anaesthesia was induced. There is presently no established rule about the best method of pre-oxygenation [1], but it seems an essential prerequisite before induction of anaesthesia. Indeed, maximal pulmonary denitrogenation with the replacement of nitrogen by pure oxygen considerably diminishes the risk of hypoxia, even if spontaneous ventilation is not maintained after induction of anaesthesia. During large inspirations and expirations with pure oxygen at vital capacity, nitrogen concentration in expired gas diminishes exponentially [2]. After eight such breaths (which need less than 60 s), the nitrogen concentration in expired gas is less than 1% allowing the patient to tolerate approximately 8 min of apnoea without desaturation (if oxygen consumption is of the order 250 to 300 ml.min^{-1}). The occurrence of desaturation can be further delayed up to 10 min by pharyngeal insufflation of oxygen [3]. As mentioned by the authors, it seems preferable to perform fibreoptic intubation under topical anaesthesia or after laryngeal block. However, if general anaesthesia is to be used, and particularly if the operator is inexperienced careful preoxygenation followed by pharyngeal insufflation of oxygen is highly desirable and should prevent severe desaturation.

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Delayed vascular puncture following axillary brachial plexus sheath cannulation

We were interested to read the article by Hill and Campbell on the use of the loss of resistance technique for identifying and blocking the brachial plexus (*Anaesthesia* 1992; **47:** 207–9). We have used this technique successfully on a number of occasions and are writing to comment on a recent complication.

A 29-year-old male patient presented for exploration of his right thumb. The axillary sheath was successfully cannulated the the first attempt with a 20 G Medicut cannula using the loss of resistance to saline technique. The cannula was advanced smoothly off the needle for about 2 cm. A T-piece extension set was attached and the cannula taped in place. After careful aspiration at regular intervals 30 ml of plain 1% lignocaine was injected into the sheath. Good anaesthesia and motor block was achieved within 15 min. There was no blood seen on aspiration at any time and the cannula was left *in situ*. Unfortunately there was a 1 h delay in commencing surgery and some motor power returned to the thumb. We decided to top-up the block with 1% lignocaine with 1:200000 adrenaline. However, on aspiration, blood flowed out freely. A 1 ml test dose resulted in the patient complaining, within seconds, of facial fullness, palpitations and a feeling of 'rush'. The pulse oximeter showed his heart rate increased from 75 to 116 beat.min^{-1}. This continued for approximately 1 min and gradually decreased. The skin incision to the thumb was pain free. A deeper incision was painful, but responded to local infiltration with anaesthetic solution.

We are aware that venous or arterial puncture during any local anaesthetic procedure is well known. In our case the cannula was not intravascular initially and yet obviously was 1 h later. We assume that the vascular puncture occurred during minor movements of the shoulder joint.

This case illustrates forcefully the need for aspiration of cannulae prior to injection of local anaesthetic, not only at first injection but also when performing subsequent topups. The delayed vascular puncture maqy have caused problems if we had commenced an infusion.

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Combined epidural/spinal anaesthesia for Caesarean section—single-space double-barrel technique

I was interested in the paper by Lyons and his colleagues (*Anaesthesia* 1992; **47:** 199–210) on the evaluation of through the needle or separate spaces for the combined epidural /spinal technique. I had been convinced of the advantages of a combined epidural/spinal technique by the work of Carrie [1], but I had, however, a number of reservations about through the needle techniques: the possibility of passing an epidural catheter into the subarachnoid space through the puncture produced by the spinal needle; the cannulation and fixation of the epidural catheter secondary to the subarachnoid administration of local anaesthetic would be likely to result in unilateral anaesthesia; the likelihood of higher failure rates with a 30 gauge spinal needle [2].

The technique I have used for the last 18 months has been the single-space double-barrel technique. After routine preparation for epidural block in the right lateral position, the 20 G introducer for a Vygon 25 G Whitacre spinal needle is inserted into the interspace as if spinal anaesthesia were to be performed in this space. The epidural space is then located using a 16 G Tuohy needle placed immediately cranial and parallel with the introducer. The epidural catheter is passed and fixed using a small occlusive dressing.

Spinal anaesthesia is achieved using a 25 gauge Whitacre needle and 2.5 ml of heavy 0.5% bupivacaine. The spinal needle and introducer are removed and fixation of the epidural catheter is completed with a larger occlusive dressing. The patients are then put into the left lateral position for a period of approximately 5 min.

Analagesia to T_4 is almost invariably obtained. Patients are ready for surgery within 10 min of the intrathecal injection of the local anaesthetic. In the last 18 months spinal anaesthesia has been unsuccessful on only two occasions, once as a result of inadequate blockade and on the other occasion due to the failure to perform the spinal puncture. However, having the benefits of the other barrel, Caesarean sections were successfully carried out under epidural anaesthesia. All patients with a functioning epidural received an opioid (phenoperidine) top-up which results in postoperative analgesia of 6–8 h.

I have reviewed my results over this period and conclude that the same space, double-barrel technique results in a rapid onset, high quality block with the advantages of epidural supplementation.

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A knotty problem with two central venous catheters

A 64-year-old Asian woman was admitted with a 4 week history of persistent cough, dyspnoea, epigastric pain and vomiting. A drug-controlled diabetic, investigations showed her to be suffering with renal failure from rapidly progressive glomerulonephritis. Though she was peritoneally dialysed, her dyspnoea worsened over the course of 3 weeks, and haemodialysis was commenced via a Vygon 'Dualyse-Cath' placed in the right subclavian vein. She continued to deteriorate and was transferred to the intensive therapy unit for ventilation, the respiratory diagnosis then being either pulmonary oedema or pulmonary haemorrhage.

To aid diagnosis and fluid management an attempt was made to site a balloon tipped, flow directed pulmonary artery catheter. The left internal jugular vein was chosen because of a haematoma in the right of the neck following attempted cannulation a few days earlier. Insertion of the 6 F sheath was achieved without difficulty. On advancing the pulmonary artery Swan–Ganz catheter, the central venous pressure waveform became damped and no right ventricular waveform appeared by 40 cm. The balloon was therefore deflated and the catheter withdrawn, but only to 30 cm before it became firmly stuck. A chest X ray (Fig. 1) showed the cause to be the coiling, possibly knotting, of the pulmonary artery catheter around the haemodialysis catheter. After discussion with the radiology and vascular surgery departments it was decided to wire the haemodialysis catheter and replace it with a sheath introducer. No longer tethered, the pulmonary artery catheter was pulled out easily. Though the patient came to no harm from this incident, she died 6 days later from her pulmonary haemorrhages.

Knotting of pulmonary artery catheters is a well-known, but uncommon, complication [1]. There have been case reports of knot formation in the great veins, pulmonary artery and, most frequently, in the heart [2]. We have only been able to find one other report of a pulmonary artery catheter knotting with another central venous catheter [3]. As in our case, the catheters were introduced on opposite sides of the body. Ensuring a good pressure waveforem, and one that is compatible with the length of catheter inserted, the normal precautions taken against coiling will not necessarily prevent it occurring around a pre-existing catheter. In view of this we seek to remind our colleagues of this danger, and suggest that careful consideration is given to placing pulmonary artery catheters on the same side of the body as any central venous catheter already *in situ*..

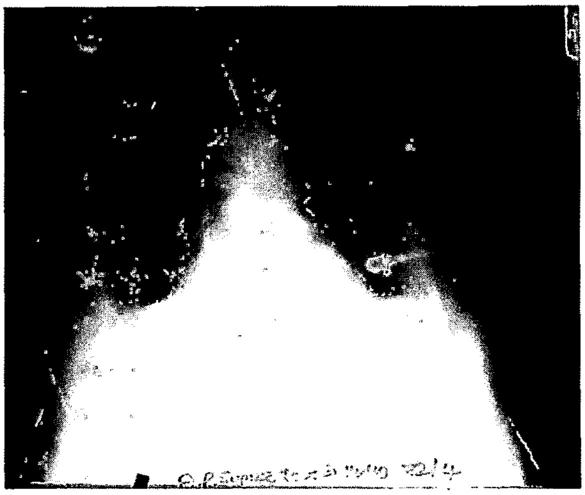

Fig. 1.

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Nitrous oxide and laryngeal mask cuff pressure

We read with interest the paper by Drs Lumb and Wrigley demonstrating an increase in intraluminal cuff pressure from 80 to 120 mmHg after 30 min of anaesthesia with 66% nitrous oxide (*Anaesthesia* 1992; **47:** 320–3). This corresponds to a mean increase in volume of 5.1 ml for a size 4 mask. It is unlikely that this increase in cuff volume and presumptive increase in pharyngeal wall pressure causes direct damage to pharyngeal structures for the reasons discussed by the authors. However, the increase in volume may have an important consequence.

Since the introduction of the laryngeal mask airway (LMA) there have been several case reports of gastric regurgitation and subsequent respiratory problems. Not all of these have occurred following inappropirate use of the LMA. Many anaesthetists are able to report their own cases of regurgitation with or without aspiration subsequent to the use of the LMA. Barker *et al.* [1] demonstrated silent regurgitation in five out of 15 patients receiving anaesthesia via an LMA, compared to 0 out of 15 patients receiving anaesthesia via a mask and Guedel airway. Rabey *et al.* [2] demonstrated a significant reduction in lower oesophageal barrier pressure after 15 min of inhalational anaesthesia in those patients with a LMA compared to those with mask and Guedel airway.

During normal swallowing, the lower oesophageal sphincter initially relaxes before contracting. The distension of the hypopharyngeal muscles by a bolus of food normally initiates this reflex. Depending on the depth of anaesthesia this reflex may be initiated when a threshold of hypopharyngeal distension is reached by the steadily expanding cuff of the LMA. Gastric contents may enter the lower oesophagus and under the influence of gravity drain into the hypopharynx.

The advice given by Lumb and Wrigley to monitor LMA cuff pressure may well be of great clinical relevance.

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Guided intubation via the laryngeal mask

Several reports describe the use of the laryngeal mask airway as a device to aid tracheal intubation. This may be achieved by passing a size 6.0 tracheal tube directly through the lumen of the laryngeal mask [1]. An alternative technique is to use the laryngeal mask as a guide to the placement of a gum elastic bougie which is then used to 'railroad' a tracheal tube into the trachea [2]. Both these techniques, however, must be queried as attempted intubation is performed in a completely blind fashion. The laryngeal mask airway may be misplaced [3] and blind passage of tracheal tube might result in trauma to the surrounding tissues. Furthermore, Payne [4] has demonstrated fibreoptically the clear inclusion of the upper oesophageal lumen within the mask opening in 6% of subjects. Passage of a tracheal tube under such circumstances may result in oesophageal intubation.

On a recent occasion we were presented with a 56-year-old female for abdominal hysterectomy whose larynx could not be visualised at laryngoscopy (Cormack and Lehane grade 4). A laryngeal mask was inserted and an airway exchange catheter placed through its lumen and into the trachea. Correct placement of the catheter was confirmed using the oesophageal detector device before any attempt was made to railroad the tracheal tube into position. In the absence of a fibreoptic laryngoscope we would advocate the use of an airway exchange catheter as a device to facilitate 'guided' intubation through a laryngeal mask airway. An additional benefit of this technique is that oxygenation may be resumed at any time during the procedure via a 15 mm adapter at the proximal end of the catheter.

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Removal of laryngeal mask airway during light anaesthesia

At the end of a minor orthopaedic procedure the size four laryngeal mask airway (LMA) was left in place, to be removed when the patient was more awake. Before regaining consciousness the patient started biting the LMA, and despite a Guedel oropharyngeal airway being in place at the same time, the LMA was transected by the patient's teeth in less than 30 s. The distal part of the LMA disappeared behind the patient's clenched teeth with the cuff still inflated. As the patient continued to breathe spontaneously through the remainder of the LMA, a volatile agent was restarted via a face mask. A few minutes later the patient was sufficently anaesthetised to allow the removal of the LMA. He made an uneventful recovery and the monitored oxygen saturation did not fall below 94% at any time. There was no damage to this teeth. In the case of damage to the inflating tube with subsequent deflation of the LMA cuff, there would be the additional risk of displacement of the LMA with possible airway obstruction.

The benefits of removal of LMAs in 'light' patients may not outweigh the potential risks, especially if the patient is transferred to the recovery ward with an LMA *in situ*.

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Freon affects infrared gas monitors

One drawback of the Normac infrared anaesthetic agent monitor is that ethanol vapour in the sampled gas causes a spurious reading [1]. The analyser is affected by the ethanol in the lignocaine spray [2] and that in the 'fruit extract' [3].

The recently introduced Brüel & Kjaer anaesthetic gas monitor, which is based on photo-acoustic spectroscopy, is not affected by alcohol [4]. However, even this new analyser has been found to be affected by the Freon in lignocaine aerosol spray [5].

The wavelength used for measurement by the new analyser is in the spectrum of 10.3–13.0 μm [4] and the wavelength of Freon is around 12.0 μm. Thus artificially high readings would be indicated immediately after tracheal intubation which has been preceded by lignocaine spray to the cords and trachea.

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A reply

Freon 11 (trichlorofluoromethanum) and Freon 12 (dichlorodiflouromethanum) are often used as propellants in lignocaine spray. It is correct that these substances absorb infrared light in different parts of the infrared spectrum, including both short and long wavelengths. Consequently, the reading of anaesthetic agents by any monitor based on infrared technology could be influenced when exposed to lignocaine spray containing Freon. The effect, though, is momentary, and the clinician would be aware of the possible misreading having just applied the spray.

Monitors measuring at the short wavelengths, about 3.3 μm, are also sensitive to Freon. Some manufacturers are even using Freon as a substitute for enflurane when the monitor is being calibrated. Brüel & Kjær have chosen to measure anaesthetic agents between 10.3 and 13.0 μm instead of in the low spectrum. Among other reasons, this is done to avoid the more pronounced and often unpredictable long acting effect of ethanol an agent readings from, for example intoxicated patients.

We would be pleased to answer any queries on this matter.

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Gas embolism during attempted laparoscopic vagotomy

A fit, 30-year-old man (ASA 1, 75 kg) underwent laparoscopic vagotomy for failure of anti-ulcer therapy. After premediction with papaveretum 15 mg and hyoscine 0.3 mg, anaesthesia was induced with fentanyl 50 μg, droperidol 2.5 mg and thiopentone 450 mg. Relaxation was achieved with atracurium 35 mg and a 9.0 mm orotracheal tube passed. Anaesthesia was maintained using enflurane and 66% nitrous oxide in oxygen, and relaxation with boluses of atracurium. Monitoring consisted of ECG, pulse oximetry, capnography, automatic blood pressure and train-of-four nerve stimulation.

Anaesthesia was uneventful for the first hour, after which the end-tidal CO_2 fell suddenly from 5.3 kPa to 1.5 kPa, maintaining normal capnograph waveform. After confirming that there was no disconnection or tube displacement, it was noted that the oxygen saturation had also fallen from 97% to 77% and ventricular ectopics had appeared on the ECG. Carbon dioxide embolism was diagnosed, laparoscopic surgery was abandoned and the abdomen was deflated. Nitrous oxide was discontinued and the patient was tilted head-down and to the left. Auscultation of the heart sounds was hampered by subcutaneous emphysema which had developed over the praecordium, and aspiration via a right internal jugular line did not yield any gas bubbles. Blood pressure was stable throughout the episode and the oxygen saturation and end-tidal CO_2 returned to pre-embolic values within 10 min. Open vagotomy was performed, anaesthesia being maintained with enflurane in oxygen. Reversal and recovery were uneventful, and neurological examination was normal on a visit 2 days after the operation.

Gas embolism is a rare complication of laparoscopy, with an incidence of 15 in 113 253 [1]. Fatal consequences can ensue, accounting for two of the four recorded in the Royal College of Obstetricians and Gynaecologists study of 50 247 laparoscopies [2]. A high risk period is during the initial insufflation of gas. Current recommendations to reduce risks include a check on the position of the insufflating needle and monitoring the gas pressure. In general surgery, dissection to identify or isolate structures may inadvertently open veins, which can admit gas if either the venous pressure is low, or the intra-abdominal gas pressure is high. This is presumably how this gas embolism occurred, at a time well after the initial insufflation, when the pneumoperitoneum was maintained by an automatic insufflator. A fall in the end-tidal CO_2 can detect as little as 0.25 to 0.5 $ml.kg^{-1}.min^{-1}$ of gas entrainment in the venous circulation [3]. The minimum monitoring guidelines recommends the use of capnography for assessing the adequacy of mechanical ventilation and in laparoscopy it can additionally warn against gas embolism. With increased interest in minimally invasive surgery, vigilance for this rare but potentially serious complication must be maintained.

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Leaking Datex sampling set for the end-tidal CO_2 monitor

In their recent correspondence (*Anaesthesia* 1992; **47:** 173), Lacoux and Christie report a case where a massive leakage was found in a patient's breathing system. The source of the leakage was the single-use gas sampling set manufactured by Datex. In fact, we did receive some reports concerning leaking sampling adapters in August 1991. When studying the case we found out that there was a defect in the molding tool used to manufacture the adapter, which caused deformation of the entrance site of the sampling tube. As a result, the tubing did not fit into the opening tightly enough to provide an adequate seal. As Lacoux and Christie correctly point out, the magnitude of the leakage varied from one adapter to another, and in the described case it was exceptionally large.

Further investigation showed that the defect had been introduced in January 1991. The fault was corrected as soon as it was located, and at the same time we instituted systematic testing of the sampling sets for leakage. Our former decision not to use this test had been based on extensive testing at the prototype phase, which did not indicate any tendency of the adapters to leak. After the problem was detected, we carefully considered the risks involved. Our conclusion was that a potential danger would be, as the writers have also recognised, hypoventilation. However, the CO_2 monitor in itself is the primary tool to detect hypoventilation. It is also worth noting that the leak will not affect the accuracy of the CO_2 measurement, because the positive pressure in the breathing system will prevent dilution of the sampled gas by room air. Therefore it was assessed that no hazard would be caused to the patient. Lacoux and Christie do not report any changes in the patient's condition due to the incident, either. We regret the inconvenience caused by this unfortunate problem, and assure that every meausre has been taken to prevent its re-occurrence.

The writers are correct in emphasising the importance of avoiding leaks in the breathing system. In this case there was a fault in the single-use sampling set, but we believe that this particular part is getting undue attention. In fact we performed some experiments and found out that with the sampling tube completely removed from the adapter, leaving a hole of 2 mm in diameter, the leak is approximately $7\ \mathrm{l.min^{-1}}$ at $10\ \mathrm{cmH_2O}$ constant pressure. To compare the leak in the reported case, one has to make some calculations: the difference of the set 700 mol tidal volume and the measured 450 ml expiratory volume is 250 $\mathrm{ml.breath^{-1}}$. At the 10 $\mathrm{breath.min^{-1}}$ frequency this gives a total leakage of $2.5\ \mathrm{l.min^{-1}}$ at a pressure of $8\ \mathrm{cmH_2O}$. Because the leakage occurs only during the inspiratory phase, the actual leak is $7.5\ \mathrm{l.min^{-1}}$, assuming a typical I/E ratio of 1:2. Without having seen the individual sampling adapter, we are convinced that the opening must have been smaller than in our test specimen, and therefore the possibility cannot be excluded that the adapter was not the only source of leak in the system. Moreover, there is no reason to believe that the single-use sampling set would as such be more likely to leak than any other part in the system. Finally, the amount of useful information achieved from CO_2 monitoring certainly outweighs the addition of the smaller connector into the breathing system.

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Allegation of sexual assault following midazolam sedation in a man

I read with interest your recent article by Drs Hosie and Todd (*Anaesthesia* 1992; **47:** 76) on the problem of persistent erection in men anaesthetised with propofol and also that propofol can cause sexual arousal in women [1]. I would like to report that endoscopy staff have similar problems in patients sedated with midazolam.

A 70-year-old man with no previous history of psychiatric or neurological illness underwent gastroscopy for dyspepsia. He was sedated with midazolam 5 mg by slow intravenous injection. The procedure was uneventful and three members of staff were always in attendance. Shortly after the endoscopy, he spontaneously reported that two female members of the nursing staff had sexually assaulted him during the procedure. One hour later he had complete amnesia for all the events surrounding the endoscopy and denied making his previous allegation.

Sexual fantasies induced by benzodiazepines have previously only been reported in women [2]. The nursing staff and I have noticed that up to 1 in 20 male patients make comments of a sexual nature to the nursing staff whilst being transferred from the endoscopy trolley to a recovery area. It is possible that many men experience sexual fantasies during endoscopy with midazolam sedation, but subsequently have amnesia, which occurs in up to 90% of patients following benzodiazepine administration [3]. These sexual comments may also result from sexual fantasies occurring during the procedure. As our patients undergo gastroscopy fully clothed I am unable to report the incidence of persistent erection during gastroscopy.

Although it is unusual for female (or male) endoscopists to be left alone with male patients, nursing staff are often in this situation and female staff should be aware of this potential risk for litigation in patients who have been sedated with midazolam.

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Basic life support performance

I refer to the letter from Dr Elias (*Anaesthesia* 1992; **47:** 357) concerning the performance of trainee anaesthetists at basic life support. There comes a time when we have to stand up for experience. If anaesthetists, who use these skills every day on people, fail to maintain an airway and ventilate a dummy adequately, logic suggests that the dummy is, to a degree, unlike a real person. The fact that they could learn to ventilate a dummy adequately with a little practice merely indicates that they have appropriate learning abilities. Dummies are no doubt essential for practice for large numbers of CPR trainees, but they cannot be used as a reliable test for performance on patients.

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False-positive aspiration tests in CVP line placement

I read with interest the report by Pina *et al.* (*Anaesthesia* 1992; **47:** 30–1) describing a case of a falsely positive aspiration test during insertion of a central venous catheter on the ipsilateral side to recent chest trauma.

I have also experienced a similar problem with a subclavian catheter, which raises the question as to whether central lines should be inserted on the ipsilateral or contralateral side to thoracic trauma.

A 24-year-old woman presented with multiple stab wounds to both upper limbs and right thorax. She was hypotensive and 1.5 l of blood was drained from a right-sided chest drain. She was brought promptly to the operating theatre for thoracotomy. After induction of anesthesia a central venous catheter insertion was attempted using the Seldinger technique via the right subclavian approach. Dark blood was aspirated and the sheath passed over the guide-wire. After connection to a giving set, dark blood was seen to pass retrogradely up the tubing. On applying a transducer to the line a flat trace of 40 mmHg was obtained, thus ruling out inadvertent arterial puncture. As a precaution, no fluids were given through the line and a second cannula was inserted into the left external jugular vein through which extra fluids were administered. At thoracotomy 2 l of blood were evacuated from the right side of the chest and the tip of the central line was found protruding through the superior vena cava into the haematoma. The line was removed and the hole oversown. Torn intercostal veins were repaired and further progress was uneventful.

There appears to be a balancing of relative risks when inserting central lines into patients with chest trauma. On the normal side of the chest it is of paramount importance not to damage the healthy lung [1,2]. Conversely, on the affected side veins may be distorted and further damage to that side of the thorax may occur, especially in an emergency in a hypotensive patient. The perforation of the pleural cavity by a central line may be unrecognised if haematoma is present and aspiration of dark blood through the line is accepted as indicating correct placement. The basic rule of first attempting central access on the ipsilateral side to chest trauma may have a morbidity of its own.

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A further persistent leak

Having read with interest the letter by Drs Hodgson and Mostafa (*Anaesthesia* 1991; **46:** 799), we would like to describe a similar incident which occurred recently.

A 20-year-old, heavily built male presented for laparotomy for suspected perforated duodenal ulcer, having been prescribed dexamethasone by a neurologist for double vision. Anaesthesia was induced, following pre-oxygenation, by a standard rapid-sequence technique with thiopentone 450 mg and suxamethonium 100 mg. The cords were easily visualised on laryngoscopy, and a 9.5 mm cuffed oral tracheal tube passed without difficulty. After transferring the patient to the operating room, anaesthesia was maintained with isoflurane in nitrous oxide and oxygen with relaxation from atracurium. The patient's lungs were ventilated through a circle absorber system, by a ParaPac ventilator giving a 'Bag-in-bottle'. Fresh gas flow was progressively reduced from 6 $l.min^{-1}$ to 2 $l.min^{-1}$ without any problems. Full monitoring was applied, including a pressure-sensing ventilator alarm.

During the procedure, a 16 FG nasogastric tube was passed with some difficulty due to the patient's build and the presence of drapes and screens. Shortly after this, it became apparent that a leak had developed in the breathing system, the bag-in-bottle collapsed followed by activation of the low limit of the ventilator alarm. A check of all connections failed to discover the problem and, as in the previous letter, more air was added to the cuff of the tracheal tube without success. Ventilation with a Waters system and oxygen cylinder still revealed a large leak. In view of the above, the tracheal tube was changed, under direct vision, over a gum elastic bougie with cricoid pressure applied. At this time, the nasogastric tube was noticed to be lying in the trachea and was removed. The procedure continued uneventfully. No defects were found on checking the cuff of the orginal tracheal tube.

This incident illustrates again the relative ease with which a nasogastric tube can pass by an adequately inflated tracheal tube cuff. In this case, in contrast to Drs Hodgson and Mostafa's experience, the patient had normal upper airway anatomy, permitting passage of an appropriately-sized tube, needing only a small cuff volume of a seal. Furthermore, the need to pass the nasogastric tube immediately after induction in the anaesthetic room, before access is obstructed by surgical paraphenalia, and to aspirate positively acid contents to confirm correct placement is underlined; this will certainly become our practice in the future.

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Atracurium block prolonged by low dose tubocurarine

The interaction of non-depolarising muscle relaxants may produce effects that are greater than additive. This potentiation may be because of differences between pre and post-synaptic actions of these agents [1]. Prior injection of the depolarising agent suxamethonium has been shown also to intensify neuromuscular blockade [2]. The combined use of relaxants with differing properties could have clinical advantages and we wish to report our experience using a small dose of tubocurarine after administration of atracurium 0.5 $mg.kg^{-1}$ in 45 patients, of ASA 1 or 2, scheduled for elective surgery requiring muscle relaxation.

All patients were aged from 20 to 89 years (mean 62.2) and weighed 44.5 to 125 kg (mean 64.7). General anaesthesia was induced using fentanyl and propofol, and tracheal intubation performed following topical lignocaine 4% spray to the larynx. Twenty-three patients received suxamethonium 75 mg for tracheal intubation, from which they were allowed to recover, and neuromuscular blockade was maintained with atracurium 0.5 $mg.kg^{-1}$. The remaining 22 patients received atracruium 0.5 $mg.kg^{-1}$ for intubation. Anaesthesia was maintained with isoflurane in 67% nitrous oxide and 33% oxygen by intermittent positive pressure ventilation. Tubocurarine 2 mg was given 10 or 15 min after the atracurium. This dose of tubocurarine is that which, if given when the amplitude of the first contraction of a train-of-four is equal to 10% of control, will produce an additional 5% block. The duration of skeletal muscle relaxation was recorded to the nearest 5 min.

In 35 patients, surgery, ended before return of muscle tone, which occurred up to 3 h 45 min after the initial injection of atracurium. Recovery of tone occurred first in only 10 patients, between 30 min and 2 h 5 min in two pyrexial subjects. It returned slowly and was usually noticed by its effect on the ventilator performance, capnograph tracing or systolic blood pressure. Mean time to recovery of tone when suxamethonium had been given (five cases) was 1 h 15 min, while without suxamethonium (five cases) the mean time was 54 min. Additional injections of atracurium 5 or 10 mg provided 29 to 30 min further relaxation. It was found an advantage during spinal decompression to be able to elicit twitch responses from nerve roots within fibrous tissue while the patient remained on intermittent positive pressure ventilation. Only one patient reacted adversely to inadvertent movement of the tracheal tube. Spontaneous breathing would often return immediately the inhalational agents were withdrawn. Reversal of the neuromuscular block with glycopyrronium and neostigmine was easy as early as 25 min after atracurium, but was not required (25 cases) when the length of the procedure exceeded 55 min.

Potentiation of atracurium may result from the inhibition of presynaptic acetylcholine release by tubocurarine, which increases potency of agents acting primarily on the post synaptic receptors [1] and is currently under further investigation. The technique described offers controlled recovery of muscle tone, the opportunity to use lower doses of atracurium and the avoidance of anticholinesterases where it is to the particular advantage of the patient.

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Intrathecal pethidine in a patient with heart block

General anaesthesia and regional blocks using local anaesthetic agents may be hazardous in patients with abnormalities of cardiac function. We describe the management of an 82-year-old man with sick sinus syndrome who underwent perineal surgery without the need for a temporary pacing wire.

An 82-year-old man presented for emergency incision of a scrotal abscess. He was known to be hypertensive and had suffered frequent falls at home. ECG recordings performed over the previous 10 years showed sick sinus syndrome with intermittent episodes of complete heart block and episodes of atrial flutter with variable block. It has been concluded that the falls were not related to the heart block and that pacing was not indicated. On examination he was mildly confused and wasted. His pulse rate was $40.\text{min}^{-1}$ and regular and arterial blood pressure was 140/90 mmHg. A 12-lead ECG revealed atrial flutter with 6:1 block, right bundle branch block and left axis deviation. General anaesthesia and conventional subarachnoid block were considered unduly hazardous in view of the cardiac conduction defect and the potential for large swings in blood pressure. It was therefore decided that a subarachnoid block with pethidine should be performed. This technique has been described in the past and has been shown to provide good sensory and motor blockade with minimal autonomic interference [1,2].

Pethidine 50 mg ($0.8\ \text{mg.kg}^{-1}$) was injected intrathecally at the level of L_{2-3} with a 24 gauge Sprotte needle. Due to the confused state of the patient, it was difficult to assess the exact sensory level of the block obtained, although after 40 min he reported loss of temperature appreciation in both legs, with an associated complete motor block, and surgery commenced. Excellent anaesthesia was obtained for the procedure and no sedation or additional analgesia was required. He was haemodynamically stable with a steady blood pressure and pulse rate of 35–40 beat.min^{-1}. The postoperative period was uneventful; pain control was satisfactory and no additional analgesia was required.

We recommend this as a useful method of anaesthesia for lower abdominal and perineal surgery, particularly in poor risk patients in whom fluctuations in blood pressure are likely to be poorly tolerated.

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Misuse of helium

It is standard teaching that in cases of upper airway obstruction, the addition of helium to the inspired gas may be of benefit, since a gas of lower density may permit a greater flow of gas when flow is turbulent. The case described below emphasises that a high $F\text{I}O_2$ is the principal therapeutic measure required when alveolar hypoventilation caused by airway obstruction is present. This must be compromised by the addition of helium.

A 75-year-old woman presented for an emergency tracheostomy; previously she had had a brain stem infarct which had resulted in bulbar palsy. A tracheostomy had been performed at that time, but her swallowing, phonation, and secretion clearance had improved to allow decannulation. After a period of several months she deteriorated acutely, presenting as an emergency with stridor, necessitating re-opening of the tracheostomy. She was given by the ward staff 21% oxygen in helium to breathe via a Hudson face mask, and was transferred to the operating theatre. On arrival she was confused, cyanosed, and pulse oximetry showed an $S\text{p}O_2$ of 45%. The Hudson mask and the 21% oxygen in helium were removed and an anaesthetic face mask applied. Oxygen was supplied at

5 l.min^{-1} from a circle system. Over a period of approximately 2 min the $Sp\text{O}_2$ rose to 96%, and the patient became lucid. There was no worsening of her stridor during this time. A tracheostomy was performed uneventfully using local anaesthesia.

This case demonstrates that there is no point in giving helium to patients with airway obstruction unless it can be given in conjunction with an appropriately high $F\text{I}\text{O}_2$. This patient would have benefited more from a high concentration of oxygen, easily administered from either the ward piped oxygen supply, or from a standard cylinder as found on operating theatre trolleys, while awaiting transfer to the operating theatre. The administration of helium, although well-intentioned and following standard teaching, was inappropriate.

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'Duck speech'

We have noted another cause for the high pitched 'duck speech' normally associated with phonation after inhalation of helium/oxygen mixtures. The patient was a 77-year-old man who had, 11 days previously, undergone transhiatal resection of an oesophageal carcinoma. He presented with a 24 h history of increasing dyspnoea and a more recent history of gross surgical emphysema of his neck and upper thorax. In addition the patient spoke with a voice indistinguishable from that described above. Nasal fibreoptic branchoscopy revealed surgical emphysema of the soft palate, pharynx and the whole of the trachea. The vocal cords were spared, but the tracheal aperture was reduced to a slit by anterior and posterior submucosal swelling. Beyond the carina, both bronchial trees were normal. Further investigation showed an anastomotic breakdown with mediastinal abcess, but no airway leak.

It is our supposition that the tracheal stenosis led to an accleration of air as the patient exhaled, forcing high velocity gas across the vocal cords and hence producing high frequency sound.

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Transdermal hyoscine

We read with interest the paper by Semple *et al.* (*Anaesthesia* 1992; **47:** 399–401) describing the use of transdermal hyoscine (Scopoderm TSS CIBA) with patient-controlled analgesia (PCA). It is documented in the datasheet for Scopoderm TSS that the equilibration between absorption and excretion of hyoscine may not be reached until 6 h following application of the patch and, therefore, maximal antiemetic effect will not be reached until this time. In this study the patch was applied only 2 h pre-operatively, and it is possible that in the critical early postoperative period maximal plasma hyoscine levels and therefore antiemetic effect, had not been reached.

In our hospital, where PCA is routinely used following major gynaecological surgery, it is our practice to apply the Scopoderm TSS patch the evening prior to surgery. We have found the incidence of nausea and vomiting to be substantially less than that quoted by Semple *et al.*, and it may be that further research into timing of patch application is warranted.

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Clonidine—a horse or an ass?

We read the editorial 'Clonidine—a horse or an ass' with interest (*Anaesthesia* 1991; **46:** 1003–4). To the extensive enumeration of the applications of clonidine to anaesthesia we suggest an addition of relevance to anesthetists working in Intensive Care. Clonidine in this respect has been used and recommended to attenuate the sympathetic overactivity of drug (especially alcohol) withdrawal states [1–3].

In the difficult terrain of such clinical 'Chevaux de Frise' we have had occasion, when thoroughbreds have failed, to be glad of the clonidine ass.

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Medicolegal and nursing practice in the private sector

Three medicolegal considerations merit attention. Firstly, the surgical/anaesthetic Consent Form. What is the legal standing of this document? Practice in the private sector varies widely. Some very reputable hospitals do not insist on its completion. Others, through the agency of their nurses, will not countenance surgery without it. It can be argued that a proposed operation is a contract between the patient and the surgeon, and legally this contract has nothing to do with the hospital, since the surgeon is not its employee in this context. Is it no more than an uncertain safeguard for each party, especially important in such areas as amputation, cosmetic surgery and minors? Has the Consent Form ever been supported or tested in the courts?

Secondly, when checking the patient at the doors of the operating threatre, it is now standard practice to interrogate the patient about his/her identity, allergies, false teeth . . . Quite apart from the stress to a patient who may have been premedicated to allay his anxiety, what view would a court take of answers given under the influence of a powerful sedative? Should not the initial check in his/her room suffice, with no more than a second identity check by wrist-band on arrival in the operating theatre? Compassion too has a place in medical practice.

Finally, there is wide variation in nursing responsibility. Some hospitals allow the nurse to administer a drug which has not been prescribed on the drug chart, provided the order (by telephone) is repeated to another nurse, and later confirmed in writing. Others, and especially perhaps less distinguished centres, will not even allow the patient an aspirin unless it is prescribed in writing, though one clinic waives this rule if the doctor also speaks to the pharmacist! What is the law? How curiously this contrasts with intensive care units which could not function without the enormous responsibility allowed their excellent nurses. I understand from the Royal College of Nursing that despite recent legislation neither National Health Service nor private (?including intensive care) nurses are allowed to prescribe anything. But does this also mean they are not allowed to accept verbal instructions? A strange situation for highly trained and esteemed colleagues.

I strongly suspect that private hospitals are especially scrupulous in adhering to the letter of the law for fear of losing their licence, a fear enhanced by such episodes as the 'kidney' scandal.

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A simple solution

Most anaesthetists are familiar with the problem of pulse oximeters either not giving any readings or only intermittently when they are needed most. These situations include hypotension and/or hypovolaemia with consequent poor peripheral perfusion [1], movement artifacts leading to false readings, hypothermia with the inability of the pulse oximeter to detect a pulse, vasoconstrictor infusions and during cardiac bypass [2]. Hypothermia is a common problem and no good solution seems to be available. Dipping the hand in warm water for a few minutes may help, but is a very short-term solution. Locally applied vasodilating creams are sometimes recommended to enhance the pulse signal in low-amplitude states [3]. We have now tried and tested a method which has always worked, unless the patient is also hypovolaemic and hypotensive.

Take a disposable hand glove and fill it with warm water (not hot) and place it in the patient's hand in such a way that the patients hand grasps the glove in a similar way as one clasps two hands together. Having done this, wait for about 2 min and apply the pulse oximeter probe to the finger; the plethysmography signal will return almost instantly. It is important to keep the glove in place throughout the period otherwise subsequent hypothermia will cause the signal to disappear again. This is a simple solution, which we learnt from our nurses and that has always worked.

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Nasal intubation and pharyngoplasty—a word of warning

A major cause of defective speech associated with congenital cleft palate is the nasal escape of air during speech. Advances in surgical technique for cleft palate closure have to a large extent overcome this problem. However, a small number of patients, following repair of the palate, have poor speech due to palatal incompetence. The most satisfactory surgical procedure to overcome palatal incompetence is the operation of pharyngoplasty. Various techniques are described but the most effective are those using a superiorly based flap from the superior constrictor muscle reflected and attached to the upper surface of the soft palate, leaving two lateral slits to form the nasal airway.

Pharyngoplasty, when necessary, is carried out in infancy. Some of these children will require wisdom teeth extraction in early adult life, an operation often carried out under general anaesthesia with nasotracheal intubation. Few of these patients will be aware of the details of their past surgery and will not give an accurate or adequate history. Normal clinical examination of the mouth is unlikely to reveal that a pharyngoplasty has been carried out. Anaesthetists and oral surgeons should be aware that patients with repaired cleft palates may have had a pharyngoplasty and that nasal intubation of the trachea may be impossible.

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A knot for anaesthetists

Surgeons, sailors and fishermen all have knots which are essential to their work and which they would each claim for themselves alone, although that claim is not always justifiable. Until now anaesthetists have not had a knot which they could claim for themsleves.

Securing a tracheal tube is a common problem for anaesthetists, either in the operating theatre or in the Intensive Care Unit. Some people use elastoplast or other sticky tape, but this is not always reliable or suitable. Narrow bandage or cotton tape is probably used most commonly and the major problem in my experience is to tie it in such a way that it does not slip along the length of the trachea tube, thereby allowing it to fall out. I have found that the Constrictor Knot (Fig. 1) is very reliable in clinical practice. It has a reputation for gripping cylindrical objects like a boa constrictor [1]. I recommend it as a knot for anaesthetists. Who knows, in time it may even acquire an eponym!

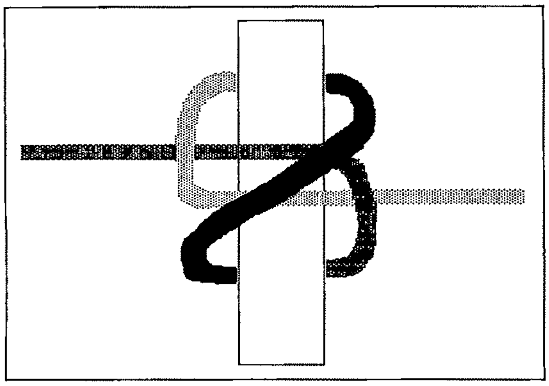

Fig 1. The Constrictor Knot: a knot for anaesthetists.

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Reference

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Publications on anaesthesia in 1847

We have been following with interest the correspondence on 'early textbooks on anaesthesia' published in 1847 [1–5]. However, no reference has been made to the catalogue by Fulton and Stanton [6], which lists 17 titles of interesting English and French publications, together with short notes, and also over 2000 bibliographies and commentaries on anaesthesia that were published in 1847. This is a very useful source of reference for historians of our specialty, which we highly recommend.

Warren [7] published his first paper on letheon in March 1847 and a further four appeared in the same year with the same title. Unfortunately, Secher [1] did not indicate to which of these he was referring. Similarly, Dinnick [4] only gives the page numbers in his reference, but from this it is possible to deduce that he was referring to the 3rd edition. We would also like to point out that in Franco and colleagues [5] reference 1, 24 should be 42, while in reference 3, 33 should be 23. In addition, the 4th edition of Morton's *Letheon* was published in January 1847.

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Erratum

Anaesthesia, 1992, Volume 47, page 450

Postpartum headache and cerebral tumour

The correct spelling of the name of one of the authors of the above letter is P.E. SIGSTON.

Anaesthesia, 1992, Volume 47, pages 824–826

Book reviews

Clinical anaesthetic pharmacology 824
Edited by J.W. DUNDEE, R.S.J. CLARKE AND W. MCCAUGHEY
Medical writing: a prescription for clarity 824
Edited by N.W. GOODMAN AND M.B. EDWARDS
Manual of postanesthesia care 825
Edited by W.K. JACOBSEN
Keytopics in anaesthesia 825
T.M. KRAFT AND P.M. UPTON

Clinical anaesthetic pharmacology

Edited by J.W. DUNDEE, R.S.J. CLARKE AND W. MCCAUGHEY. Pp. 640. Churchill Livingstone, 1991. £60.00.

The preface introduces this book as a practical guide as well as being a basic text. It is of course very difficult in a book of this size to do both of those things and there is a risk that an attempt to cover everything will end with inadequate coverage of many items. This book does not, however, fall into that trap and is well balanced overall. An inspection of the contents page reveals just how comprehensive is the coverage, with all the commonly expected topics included. A preliminary section on background matters includes chemistry, pharmacodynamics and pharmacokinetics. It is good to see a section on the topical issue of the influence of age on drug action. The sections on the influence of liver disease and cardiovascular disease are, however, very disappointing, although that on renal disease makes worthwhile reading.

The remainder of the book is divided into five major sections, the first four of which concern drugs acting on the central nervous system, peripheral nervous system, cardiovascular system and other systems. Looking at the individual chapters that make up each section it is hard to single out any particular one as outstandingly good or bad. They are all comprehensive and make interesting reading. As one might expect from a knowledge of the interests of the senior author, the sections concerning intravenous anaesthetic agents are thorough. The last section is entitled 'Special drug problems in patient management' and includes pregnancy, electrolytes, parenteral nutrition, adverse reactions, drug interactions, overdoses, and analytical matters. There is also a chapter on clinical trials in this section which contains information otherwise difficult to find.

The book is clearly aimed at the candidate preparing for the Part II Fellowship examination, and contains a wealth of useful information. It does not, however, contain everything the candidate needs to know and additional texts will still need to be consulted in order to consolidate knowledge.

Throughout the book there are a few disappointing errors or omissions. Monocomponent insulins are given only a passing mention and the reader is led to believe that the bovine insulins are still the principal agents. There is no mention of sucralfate in the management of gastrointestinal ulceration. These points may be a reflection on the long gestation period of the book.

All in all, this book is a worthwhile addition to the literature. It has been long in development but the end result has been worth waiting for.

B.J. POLLARD

Medical writing: a prescription for clarity

Edited by N.W. GOODMAN AND M.B. EDWARDS. Pp. 190. Cambridge University Press, 1991. £12.95.

It is an apparent paradox to welcome the publication of a book for which there is no need. In this instance, one has to recognise that other good texts with similar objectives already exist. Any doctor who is really serious about improving the quality of his or her writing could find several suitable books. The evidence that they do not do so lies strewn across the desks of Journal sub-editors and some examples even leak into print. Take the following opening sentence from the summary of a paper published in *Anaesthesia* earlier this year. 'Upper oesophageal sphincter pressure has been measured in 24 patients with a sleeve device. The median sphincter pressure when awake was 38 mmHg, and when anaesthetised and paralysed was 6 mmHg'. A literal minded reader might wonder if the sleeve device which these patients had was, perhaps, an arm and how you can tell when a median sphincter is awake. In an age in which Admission Officers do not expect entrants to Medical School to be able to spell and a post-Fellowship doctor can be appointed as a Research Fellow before anyone notices that he is dyslexic, perhaps one should not be too surprised.

If its mere existence encourages some people who would otherwise not have done so, to read a book of this kind, it will have served its purpose. If they read this example of the genre, they will certainly become much more critical of what they read and what they write.

This paper-backed slim volume is structured as a metaphor for illness and is divided into three parts: Part 1. Problem: the illness, Part 2. Solution: symptomatic relief, and Part 3. Practice: recuperation. Of these, the first is short and really unnecessary. People who have got as far as opening the book will either already know that their writing could be improved, or have been told so. Part 2 is the important section and consists of published examples of jargon, verbosity, or other literary solecisms, followed by the authors' rewording of them. The titles of the chapters will give you the flavour: Guidelines to clearer writing; Is there a better word?; Superfluous words; Imprecise words and phrases; Superfluous phrases; Trouble with short words; Use of the passive voice; Consistency: number and tenses; Circumlocution; Word order and pronouns; Punctuation; and Constructing sentences.

One of the most useful elements is a list of danger words which signal a sick sentence. The authors suggest that if you use a word processor for writing you can put these in a 'SEARCH' list. It seems to me that the tyro also needs a program which links any suspect word to a short piece of text which explains why it *is* suspect and how to handle the problem.

This book may have less long-term impact than it deserves at the individual level. As long as poor quality writing gets published, there is insufficient incentive to improve, other than pride in one's product. I hope, therefore, that journal editors will read it and be moved to reject even good science if it is poorly expressed. What a hope!

M.D. VICKERS

Manual of postanaesthesia care

Edited by W.K. JACOBSEN. Pp. 246. W.B. Saunders, 1992. £17.50.

This book was written to assist anaesthesia residents, nurses and respiratory therapists in their care of patients in the postanaesthesia care unit (PACU) and is clearly aimed primarily for the American market. The concept of PACUs, where patients apparently remain for considerable periods of time, may be less familiar to anaesthetists in the UK, where most recovery units are not equipped for long-term admissions and patients are generally transferred to ICUs if recovery complications are either prolonged or anticipated. By including a wider range of conditions, more commonly associated with intensive care, the depth of discussion has necessarily been curtailed and is insufficient for anaesthetists studying for the postgraduate examinations. However, for those beginning a career in anaesthesia, this book supplies much valuable information about the major postoperative complications with which they will be confronted and will provide a useful framework on which to build.

The topics discussed are divided into chapters by organ systems, each describing the common problems seen postoperatively, their likely causes, diagnosis and treatment, all set out in a clear and logical manner which is easy to follow. Other chapters are devoted to specific entities such as nausea and vomiting, body temperature, pain management and discharge from the PACU. The 14 contributors are all from the Loma Linda University School of Medicine in California and this has clearly contributed to the welcome consistency of style throughout the 18 chapters. There are no diagrams, illustrations or references, but each chapter is followed by a list of suggested reading, mostly American in origin.

The index is sufficiently comprehensive to enable practical advice on most problems to be easily accessible and this will no doubt be of particular value to less experienced staff. In clinical situations where emergency drugs may be required at short notice there is great merit in the use of familiar names. The use therefore of American Pharmacopeoa names will restrict its value to many British readers, although this could be overcome if an appendix with UK equivalents were to be included in future editions. The book contains a wealth of sound, practical advice, set out in a clear and logical fashion and there are no obvious omissions. It would be of great value to nursing staff responsible for the care of patients postoperatively, not only in recovery units and PACUs but also in surgical wards. Although it was not written specifically for housemen, I feel this is the group who might benefit most from this text, especially those working in hospitals less well-endowed with recovery facilities.

Advances in surgery and anaesthesia have led to increasing demands on the care required for patients in the postoperative period. A clear understanding of the problems likely to occur in patients recovering from surgery is vital for those responsible for their care so that they can be anticipated and avoided before they become uncontrollable and irreversible. This book can be recommended to all those seeking to improve their performance in the day to day care of patients following surgery.

R.J. ELTRINGHAM

Key topics in anaesthesia.

T.M. CRAFT AND P.M. UPTON. Pp. xiii+298. Bios Scientific, 1992. £14.95.

This is a bold and quite successful attempt to deal with a very wide range of subjects by a common format. The preface disarms criticism by disclaiming comprehensiveness and acknowledging that some of the chosen topics do not fit the format. I could not help being reminded of the small print on my skiing holiday insurance—the sort of thing that the Consumer Association gets so wound up about.

In 300 pages of pleasantly readable, well-laid out text, the authors present information on 100 anaesthetic and related medical topics varying from adrenocortical disease to vomiting by way of brain death, CEPOD, dental anaesthesia, positioning the surgical patients, pyloric stenosis and scoring systems. One or two references, either to standard textbooks or to relevant articles are suggested as further reading for most topics. On the whole, these are sensible. There are no illustrations. A list of abbreviations is provided and an excellent short section on monitoring precedes the topics. I would have liked to see a similar statement on the requirements for skilled nonmedical help during the conduct of anaesthesia; I do not think it is mentioned anywhere, although reference to the need for senior or additional anaesthetic help is usually appropriately made. I cannot claim to be knowledgeable, let alone an expert, in such a wide range of subject matter and I envy the assurance of two senior registrars who, with acknowledged help, display such confidence. I found the treatment of post-tonsillectomy haemorrhage narrow and outdated: in a good unit 40% of children certainly do not lose 10% or more of their blood volume and it is inappropriate to give a 1964 reference for this topic since anaesthetic and surgical techniques are vastly different and, above all, close recovery supervision now more or less ensures that children are well resuscitated and returned to the operating theatre promptly; the use of blood transfusion should be an extreme rarity. I was rather surprised that, in dealing with laryngectomy and tracheostomy, no mention is made of the problem of surgical damage to the tube cuff.

Silly slips irritate the pedant in me: pressure is not force x area (p 197) and I hope the risk of HIV infection is not 1 in 6000 units (p 5)—a recently quoted figure of 1:61 000 for the US is bad enough. There is also some sloppy use of terms; I don't believe that the incidence (as opposed to the prevalence) of asthma is 3–6% (p 76), intubation for drug overdosage is not 'awake' (p 125) and a nasopharyngeal pack is hardly the way to maintain a clear nasal airway (p 72). I am also sad that so many cliches are repeated uncritically: gallamine is not especially prone to placental transfer, one unit transfusions should certainly be used if they are the sensible minimum to bring a patient to a safe state and, worst of all, the tongue does not fall back into the oropharynx on induction of anaesthesia. This latter statement appears under the heading of *pulmonary* (my italics) sequelae of general anaesthesia and the suggested further reading is an excellent editorial by Drummond in which he is at great pains to correct this common misrepresentation of the major cause of upper airway obstruction. Textbooks have been described as archives of unexpurgated tradition and maybe the authors' excuse is that these are the answers expected by examiners? Certainly, all examiners should read this book since it represents a perception of the Parts I and III that they might like to consider carefully.

Despite my criticisms (and the fact that Rosemary Mason's *Anaesthesia databook* uses a similar format but is comprehensive, up-to-date and provides much more help for the clinical anaesthetist) this book may well provide just the right approach for the weary, dispirited and work-immunised examination candidate. I can envisage a non-anaesthetist partner using it to construct questions when even reading has been rejected! When the candidate revives a little he or she will be quite capable of challenging and expanding its contents.

M.L. HEATH

THIS PAGE CONCERNS YOU IF YOU ARE A MEDICALLY QUALIFIED ANAESTHETIST IN GREAT BRITAIN AND IRELAND, OVERSEAS OR IN TRAINING AND ARE NOT YET A MEMBER OF THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND OR IF YOU ARE A MEMBER OF ANOTHER PROFESSION WHO PRACTISES IN ANAESTHESIA AND YOU WISH TO APPLY FOR ASSOCIATE MEMBERSHIP

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The right of attendance at the Annual General and Scientific Meetings and all other meetings of the Association of Anaesthetists.

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Fill in the application form on the other side of this page.

Have it countersigned by two members or the Association, one of whom must be an Ordinary Member.

Tear out the page and send it to the address indicated overleaf.

Do not send money with your application

THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND

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9 Bedford Square
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(This application will be considered by Council at its next meeting. NO MONEY should be sent in the meantime. After acceptance of the application by Council, the Hon. Secretary will notify the applicant of Council's decision and the amount of subscription payable in the current financial year).

.... 19

The Honorary Secretary
Association of Anaesthetists of Great Britain and Ireland

I (full name) .... offer my name as a candidate
BLOCK LETTERS
for (a) ORDINARY MEMBERSHIP (b) OVERSEAS MEMBERSHIP (c) ASSOCIATE MEMBERSHIP (d) TRAINEE MEMBERSHIP of the Association *(please delete categories not applicable)**

I hold the following appointment(s) as an anaesthetist *(please state grade if in National Health Service, and indicate the approximate proportion of time spent in the practice of anaesthesia)*:

....

....

....

Qualifications (with dates)..

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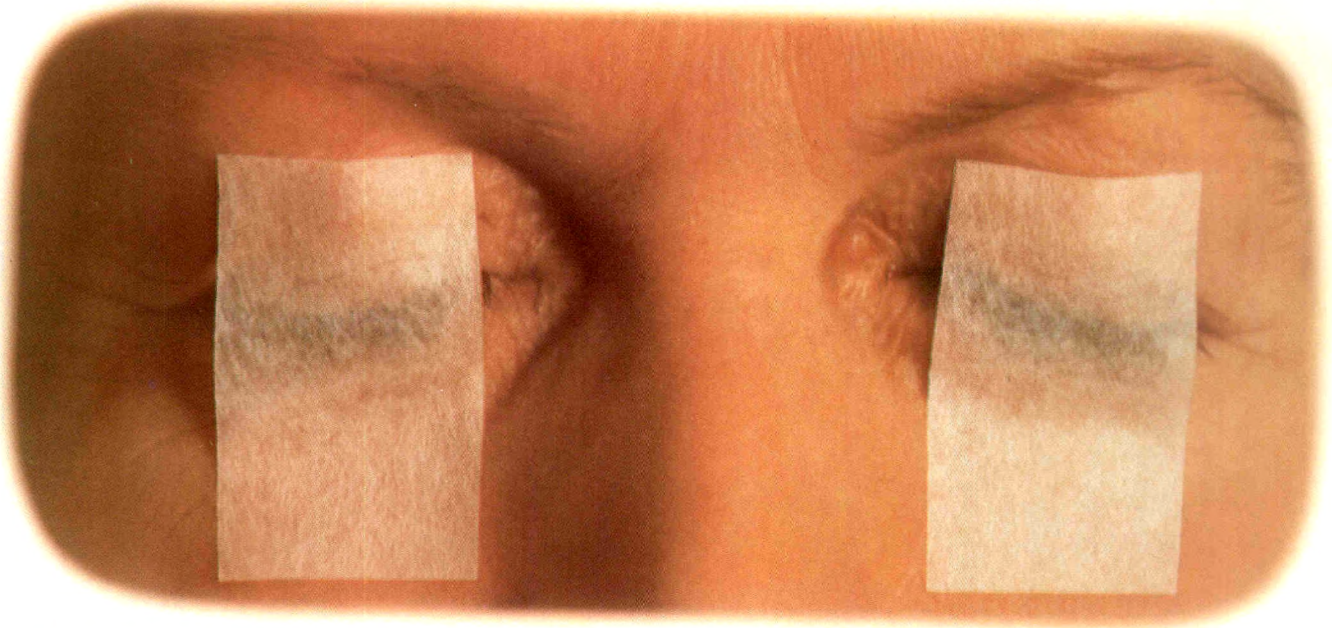
HOW CAN A HIP OPERATION AFFECT THE EYE?



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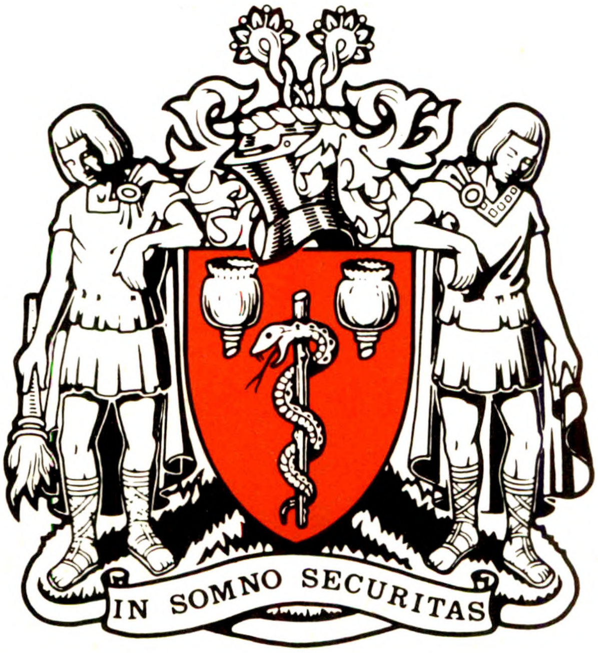

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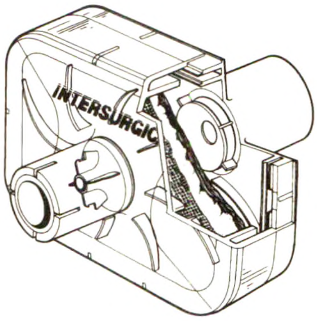


The extent to which a breathing filter will allow the passage of liquids can affect it's efficiency as a microbial breathing filter.

There are two circumstances where a filter is exposed to a liquid threat:

- In a humidified system, where the filter protects the ventilator from contamination. (It is quite normal to see liquid on both sides of a filter in these circumstances due to a build up of condensation - this does not mean that the filter has been compromised).
- Exposure to liquid secretions and or blood from the patient.

The Intersurgical filter medium is made from a hydrophobic material which is resilient to both of these liquid challenges. In fact, during independent tests the Intersurgical filter medium was challenged by contact with an increasing volume of contaminated condensation over 24 hours and returned an efficiency of 99.999%.(1) and a resistance of never more than 2.2 cm H_20.(2)

No, the Filta-Therm and Filta-Guard do not leak liquids or 'wet out' on contact.

The Intersurgical filter medium will, however, allow the passage of liquid at a pressure differential of approximately 8-10 cm H_20.

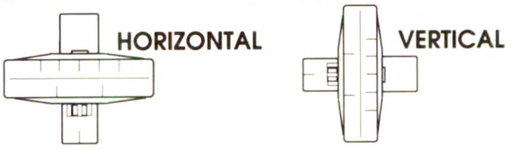
Oh dear! but don't pressures in breathing systems often exceed this?

Yes, but this pressure is **not** acting on the filter medium.

Gas does not create pressure until it meets resistance, and the maximum resistance of the Intersurgical filter is 2.2cm H_20 even after 24 hours at 60 lpm in 98% relative humidity (see the latest HEI report on HME's). This is far too low a pressure drop for liquids to be forced through the filter medium. Even if the filter is half full of liquid, gas takes the path of least resistance, which is still less than 2.2cm H_20.

Try not to think of pressure in these circumstances as a column of liquid on the filter medium. This does not represent the situation in the breathing system.

The only way in which a substantial pressure drop can be created across either Filta-Therm or Filta-Guard is by total liquid occlusion of their surface.



This is most unlikely in normal clinical use since in a vertical plane liquid runs away via the connector ports before the product becomes even half full. A liquid occlusion may happen in very rare circumstances, say a large pulmonary oedema whilst a filter is being used in the horizontal plane.
This would normally be noticed and the filter changed, but what happens if it is not?

A filter that is totally impervious to liquids, may act as a one-way valve. Allowing gas to, but not away from the patient this would quickly result in pressure damage to the patient's lungs.

On the other hand the Intersurgical filter is designed to allow the passage of liquid in such exceptional circumstances. This may result in a "dirty" breathing system but the patient is safeguarded at all times.

We feel that this is the ideal balance of hydrophobic properties.

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(1) Bacterial/Viral Test Protocols CAMR, Porton Down
(2) HEI Report No.111

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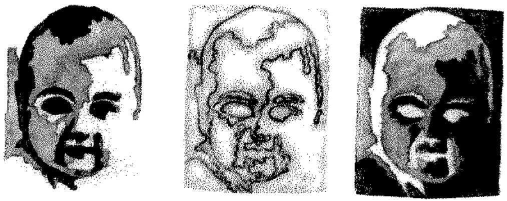

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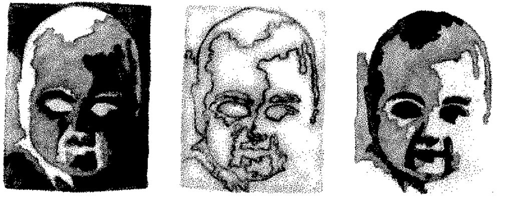

IN INFANT HEART SURGERY

The Royal Brompton National Heart and Lung Hospital, The University of Gothenburg and Gambro Cobe are sponsoring a two day symposium relating to the neural, systemic and other non-cardiac effects of profound hypothermia in infant cardiac surgery.

Further information can be obtained from The Postgraduate Centre, National Heart and Lung Institute, Dovehouse Street, London SW3 6LY, England.
Telephone: 071-351 8172 (24hr answering service)
Facsimile: 071-376 3442

How to defend the defenceless.

Gram-negative sepsis is a deadly disease. Epidemiological studies indicate that the incidence of Gram-negative sepsis is increasing due to the widespread use of potent antibiotics, invasive surgical procedures, and an increasing number of immunocompromised patients.[1]

The disease progresses rapidly – organ failure can occur within hours[2,3] – ultimately leading to death. Prompt, aggressive treatment is therefore necessary. That is why the early administration of Centoxin (HA-1A), an anti-endotoxin, human monoclonal IgM antibody – is vitally important.

Clinical data shows that Centoxin provides significant and sustained reduction in mortality in septic patients with Gram-negative bacteraemia – particularly those with septic shock.[4] It has also been found to be safe and non-immunogenic in clinical studies to date.[4]

ONE DOSE/**HUMAN**/IV

CENTOXIN® ▼

(HA-1A)

Saving lives in Gram-negative sepsis and septic shock

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Abbreviated Prescribing Information and References, see overleaf.

CENTOXIN®

Abbreviated Prescribing Information

PRESENTATION Centoxin is a solution for intravenous infusion after dilution with normal saline. Each vial contains:
HA-1A 100 mg/20 ml

USES Centoxin is indicated for the treatment of patients with the sepsis syndrome and a presumptive diagnosis of Gram-negative bacteraemia, especially those with septic shock. Centoxin therapy should be given in hospital, along with the appropriate antibiotics and supportive therapy, as soon as Gram-negative sepsis is clinically suspected. Centoxin should be given once and is not intended for repeated use.

DOSAGE AND ADMINISTRATION The recommended dose of Centoxin is a single 100 mg intravenous infusion. Centoxin should be administered intravenously over a period of 15 to 30 minutes in a total volume of 70 mL after dilution with normal saline for injection. In patients studied to date, it has not been necessary to adjust the dosage for renal or hepatic function.

CONTRA-INDICATIONS, WARNINGS ETC. Contra-indications Centoxin should not be used in patients whose primary injury involves burns, since no studies have been done in those patients. Centoxin should not be used in patients with known hypersensitivity to murine proteins. Centoxin should not be used in patients with previous exposure to HA-1A.

Undesirable Effects No serious or life-threatening adverse reactions attributable to Centoxin were reported among the more than 300 patients who received the product in clinical trials, including more than 45 patients who received 200 or 300 mg of HA-1A as a single dose. Transient flushing, localized urticaria and hypotension have been reported rarely (<1%) in patients receiving Centoxin. Human antibodies against Centoxin have not been detected.

Special Precautions *In vitro* and *in vivo* mutagenicity studies have not demonstrated any mutagenic effect. Studies have not been performed to evaluate the carcinogenic potential or effects on fertility in male or female animals. The use of Centoxin in children has not been extensively studied. Centoxin has been administered to a small group of children (ages 10 months to 13 years), the majority of whom had fulminant meningococcaemia with shock and purpura. The dose administered was up to 6 mg/kg to a maximal dose of 100 mg. Centoxin was well tolerated by all patients. The efficacy of Centoxin in adults and children with meningococcal septicaemia has not been established and therefore the use of Centoxin in meningococcal septicaemia cannot be recommended. Centoxin contains a murine J chain, which suggests that anti-HA-1A antibody formation is a possibility. Nevertheless, in clinical trials, anti-HA-1A antibodies were not detected (with a radioimmunoassay) in blood samples taken from patients up to 35 days after administration of a single dose of Centoxin. The immunogenic risk of repeated administration of Centoxin has not been extensively investigated.

Use During Pregnancy and Lactation There has been no experience to date with the use of Centoxin in pregnant patients, and animal reproduction studies have not been conducted. Therefore, Centoxin should be used in pregnant patients only when, in the judgement of the physician, anticipated benefits outweigh the potential risks. It is not known if Centoxin is excreted in human milk.

Interaction with Other Medicaments and Other Forms of Interaction There have been no reports of interactions between Centoxin and other drugs used concomitantly in the treatment of Gram-negative sepsis.

Overdose The maximum amount of Centoxin that can safely be administered has not been determined. However, single doses as high as 300 mg of Centoxin have been safely administered to adults, and doses of 6 mg/kg up to a maximum of 100 mg to children from 10 months to 13 years of age.

Effects on Ability to Drive and Use Machines HA-1A is pharmacologically inert and can therefore not be expected to affect the ability to drive and use machines. It is, in any case, administered only to hospitalized, seriously ill patients.

LEGAL CATEGORY POM.

PACKAGE QUANTITIES Centoxin is available as a package containing 1 single dose 20 ml vial.

Product licence number 8563/0010.

Basic NHS cost £2,200.

Date of preparation May 1991.

For further information refer to data sheet or contact: Centocor Medical Services, Centocor B.V., Einsteinweg 101, 2333 CB Leiden, The Netherlands. Tel. 0800-898458 (UK), 1800-55-3103 (Ireland).

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1. Centres for Disease Control: Increase in national hospital discharge survey rates for septicaemia. *Morbidity and Mortality Weekly Report.* 1990; 39: 31. 2. Kreger, B.E., Craven, D.E., Carling, D.E., McCabe, W.R., *Am. J. Med.*, 1980; 68: 332-344. 3. Straube, R., International Congress for Infectious Diseases. Montreal, Canada. July 15-19, 1990. (Abstract No. 99). 4. Ziegler, F.J., Fisher, C.J. Jr., Sprung, C.L., *et al.*, *N. Engl. J. Med.* 1991; 324: 429-436.

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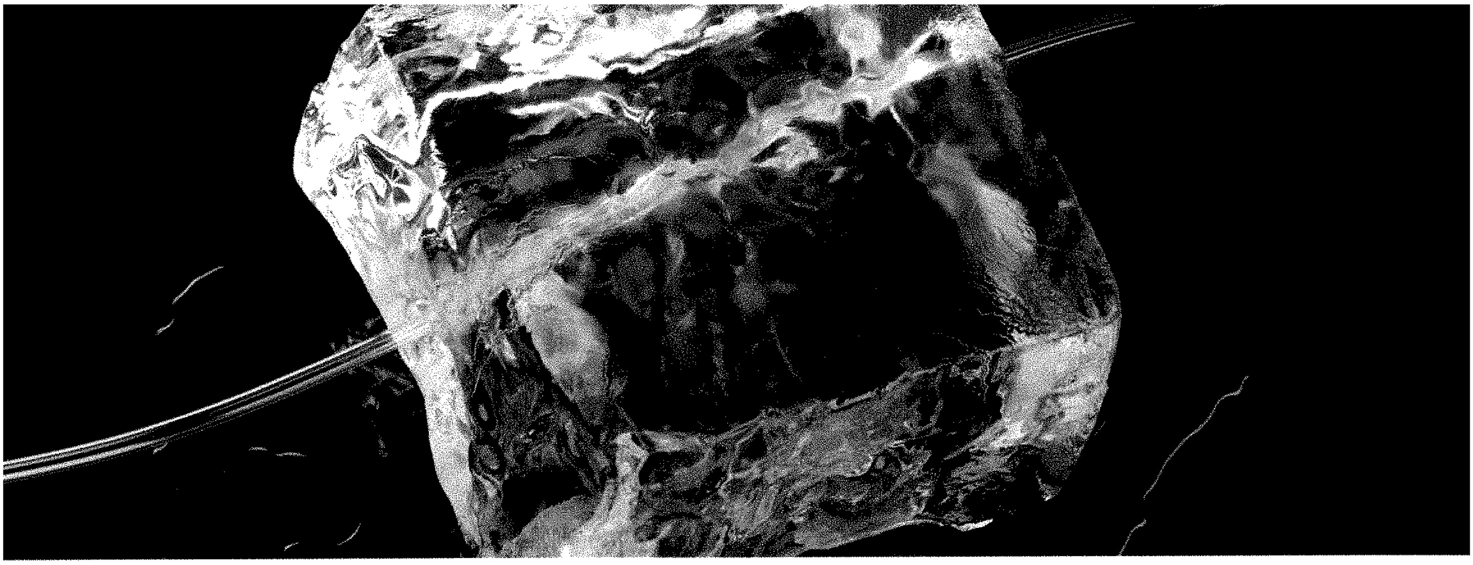

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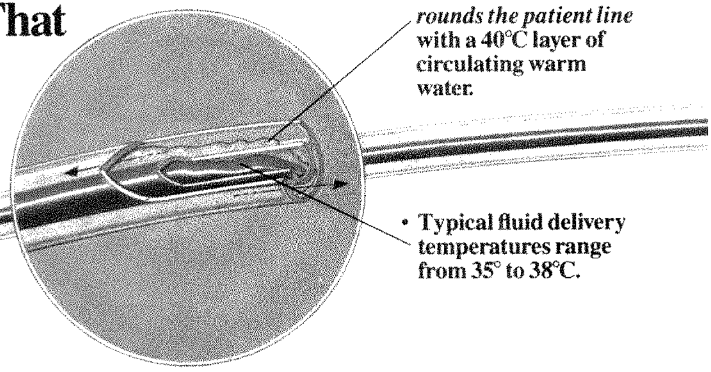

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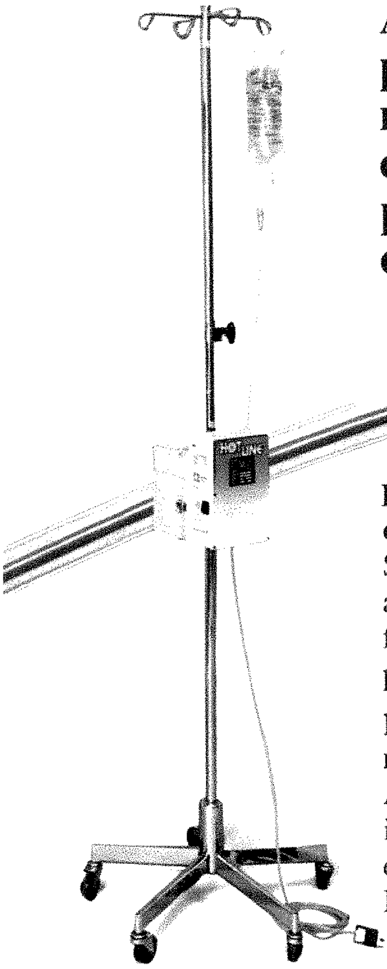

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Anaesthesia, 1992, Volume 47, pages 827–828

Editorial

Twin challenges

The way ahead is clouded — has it not always been so?

The arrival of each new President of the Association of Anaesthetists of Great Britain and Ireland poses different problems for the holder of the post and for those who have to support the incumbent during the ensuing 2 years of office.

It is a rare pleasure to begin by acknowledging the formation of the Royal College of Anaesthetists and the celebration of this event on 5 October 1992. I must also indicate both how pleased I am to see our academic body joining the other Royal Colleges and how privileged I have been to be present and active in both bodies to witness the latter stages of evolution. This is the end point of many years of work by many dedicated anaesthetists to whom we owe our thanks and who can now savour the fruits of their labours.

Perhaps now, more than ever, there is a need for anaesthesia and anaesthetists to have at least two bodies working hard on their behalf on the many problems which are on the horizon. Careful handling both politically and educationally is essential as the place of the anaesthetist which has been fought for over many years by our distinguished predecessors must be protected at a time when great pressures are being placed on all members of the medical profession. I have no anxieties that we will cope with the challenges which present, but care must be taken to ensure that the end result while fair and just for the patient does not eliminate us on the way!

Having indicated that there are two bodies working for anaesthetists and for anaesthesia does not mean that I am unaware of the diligent and painstaking work done by the many specialist societies which have emerged and the liaison which these groups have forged with other closely related disciplines. These societies too have a vital part to play in the continuing development of the activities of anaesthetists which are so clearly no longer restricted to blowing a bit of gas over someone else's patient. Nevertheless, we must constantly remind ourselves that in spite of the efforts and monies devoted to educating the public about our activities there continues to be a great dearth of knowledge on the part of the aforesaid public as to what we actually do and indeed even who we are. Every anaesthetist has a responsibility to overcome this problem; central bodies can only do so much.

Two challenges are mentioned in the title. The first relates to the interface between our specialty and the developing National Health Service, of which we are all proud and anxious to see our money — not the government's money — being used to the best advantage. Your Association has a responsibility to encourage its members to contribute to improvements in the Health Service — as it has always done, and to assist and encourage hospital management to advance this concept.

Anaesthetists can have a valuable role to play. Long hours in the operating theatre create an awareness both of the needs of operating theatre services and the competing claims of operating theatre users. Anaesthetists are also relatively independent of the competing demands and able to give unbiased advice. This perhaps explains why so many anaesthetic departments and anaesthetists are assuming management responsibilities.

While the Association wishes to encourage anaesthetists to take on these duties and responsiblities it is extremely important to ensure that the anaesthetists who do so are provided with the necesary administrative support to allow them to undertake the requisite tasks. Anaesthetic departments have over the years been starved of secretarial assistance because it has not been appreciated how much administrative work is involved in running an anaesthetic service, far less a clinical directorate. It is not acceptable, as has been reported on a number of occasions, for managers, frequently well supplied with secretarial and administrative support, to attempt to devolve on anaesthetic departments large sections of their responsibilities without transferring even the already existing resources. Your Association hopes to provide guidance and advice on these matters in the not too far distant future.

At the same time it is necessary for the Association to advise its members how services may be streamlined and made more efficient without the specialty of anaesthesia becoming unattractive to potential recruits. As one of the so-called 'service specialties', directly involved in patient care, it is a fact of life that unless guidelines are laid down for the provision and use of our skills, other disciplines which increasingly request our time, will continue to be unaware of the totality of demand. With financial pressures bearing heavily down on medical appointments the result may be an excessive clinical commitment. Anaesthetists who find themselves in such circumstances should be very wary when offered short-term financial inducements to undertake additional clinical and administrative tasks.

In recent years there has grown a sudden awareness of the pressures which medical advances have placed upon trainees and it has become clear that their hours of work and continuing commitment must be guarded and controlled if they are to work efficiently and safely. I wonder how many consultant anaesthetists on a nominal 38.5 h clinical contract would wish to receive the same consideration! Senior members of the medical profession they may be, thought of as well paid, able to do private practice, but who has appreciated the many hours they spend caring for patients, the many hours on-call, the many hours at committees, arranging rotas, sorting out problems? When it comes to the time for hours for consultants to be more clearly defined the situation is frequently dismissed — the work has always been done that way, so it is assumed to be normal. Anaesthetists are no more immune from these views and opinions than consultants in other disciplines which may be less clinically arduous.

The second limb of the challenges ahead on which I wish to comment relates to the involvement of the United Kingdom with the European Community.

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Arrangements for medical training at all levels from the undergraduate to the specialist are different in every country of the European Community. The nearest country to ourselves in this respect is the Republic of Ireland. Many other countries of the Community diverge widely in these fields and some are so different as to be unrecognisable. However, it is the view of the European authorities that specialist training within all the countries of the European Community is comparable and no difficulties are anticipated over the free movement of doctors and indeed specialists between its member states. That this is manifestly absurd does not seem to have registered until recently.

It has now been decided that the way to overcome the problem of dealing with the variations in training structures is to set up European Boards in all specialties and to empower these groups to provide the necesary solutions. This is a clear example of 'closing the stable door after the horse has bolted!' In any case, there is at this time no evidence that these new European Boards will be given any real administrative clout or resources with which to act.

The Boards are envisaged to include representation both from the National Association of each member state and from its National Scientific organisation. As far as the United Kingdom is concerned this poses no great problem with Association, Royal College and Faculty representation available, but this clear representation is much more difficult to organise from some other countries in the European Community where national associations are less representative and scientific activity is based not on a national body but upon a number of university centres. It will be interesting to see how the situation develops.

Is it important? It certainly is if all the countries of the European Community are to offer similar standards of medical care. Frequently we forget that the National Health Service, by offering the same terms and conditions of service and demanding the same standards of training over the whole country is able to recruit excellent individuals to all hospitals regardless of their geographical location. While in some countries of the European Community very high standards of care are available in the large University Teaching centres, there may be weaknesses in staffing in some of the more peripheral centres. Will the introduction of competing Trusts produce a similar situation in the UK?

Furthermore, it is now clear that we have devoted too much effort to restricting the number of trainees we are producing. A number of countries in the European Community produce very large numbers of medical graduates who subsequently become unemployed and for whom free movement throughout the European Community to countries which are less profligate with their training may be very attractive.

Your Association through its Council is well aware of these and other similar problems and is working hard on your behalf to offer constructive advice to its members and to all who will listen. I am sure it will not lack the will to continue to provide the necessary advice to those whose support it seeks.

W. R. MACRAE
President
Association of Anaesthetists of
Great Britain and Ireland

Editorial notices

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979: **1:** 432 5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of most issues.

Anaesthesia, 1992, Volume 47, pages 829–831

Does the laryngeal mask airway compromise cricoid pressure?

T. I. STRANG

Summary

The laryngeal mask airway was inserted in 10 cadavers. At postmortem the chest was opened and an infusion set primed with a dilute barium solution was inserted into the oesophagus and ligated in place. A cricoid force of 43 N was then applied and the infusion set was positioned so that when the clamp was opened it generated a pressure of 7.8 kPa within the oesophagus. The cricoid pressure was able to stop the flow of fluid into the oesophagus. This demonstrates that cricoid pressure is effective in preventing reflux at intragastric pressures which are encountered clinically and the presence of the laryngeal mask airway does not compromise this.

Key words

Larynx; cricoid pressure.
Equipment; laryngeal mask airway.
Complications; regurgitation.

The laryngeal mask airway (LMA), which was first introduced in 1988 [1], has been used extensively to provide a safe airway in spontaneously breathing patients who are not at risk from aspiration of gastric contents. Recently, Chadwick and Vohra reported its use in conjunction with cricoid pressure, in a patient who was at risk from pulmonary aspiration, when failed intubation occurred at emergency Caesarean section [2].

However, the effectiveness of cricoid pressure in the presence of a correctly positioned LMA has not yet been established.

Method

Consent to undertake this investigation was obtained from the coroner. Postmortem examination began with removal of the anterior chest wall to expose the lungs and mediastinum.

An LMA of appropriate size was inserted according to the manufacturer's instructions [3]. Correct positioning was confirmed by (i) fibreoptic endoscopy, (ii) observing inflation of the lungs and (iii) palpation of the mask in the neck.

The oesophagus was then incised 3 cm below the level of the cricoid cartilage. A standard infusion set was modified by cutting off the distal 5 cm of tubing and creating an additional 2 mm lateral orifice, 0.5 cm from the distal end. The infusion was then primed with a dilute saline–barium mixture and the modified end was inserted into the proximal oesophagus which was then ligated around it.

The cadaver was positioned with the lower cervical vertebrae flexed and the atlanto-occipital joint extended; the classical 'sniffing the morning air' position used for tracheal intubation.

A cricoid force of 43 N was applied using a latex mould of the author's neck, which overlay the cricoid cartilage of the cadaver and supported a 4.4 kg lead mass. The apparatus was held in place, being careful that no additional force was transmitted onto the cricoid cartilage by the author's hands.

The infusion was then positioned so that when the clamp was opened it generated a pressure of 7.8 kPa up the oesophagus. The accuracy of this pressure had previously been verified with a water manometer. The infusion was started whilst cricoid pressure was maintained and the inspection chamber was observed for evidence of flow. After cricoid pressure had been released, evidence of flow was once again sought (Fig. 1).

Results

Insertion of the LMA was possible in all four male and six female cadavers. In all 10 cadavers the lungs could be

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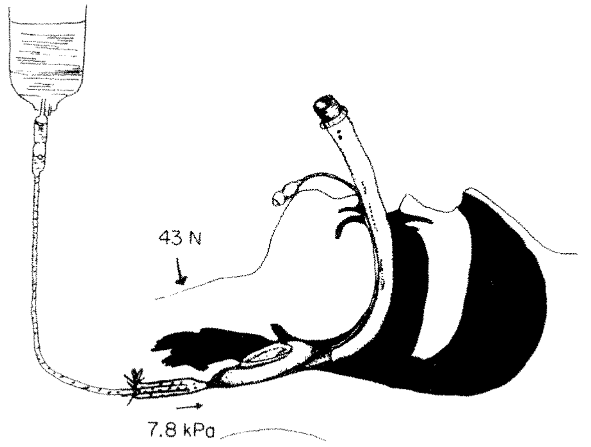

Fig. 1. Lateral view of the laryngeal mask airway in place and the infusion set ligated in the oesophagus. Horizontal arrow indicates a pressure of 7.8 kPa within the oesophagus. Vertical arrow shows a cricoid force of 43N applied in the neck.

inflated though the LMA and the upper part of the cuff could be palpated through the thyrohyoid membrane. In nine cases a bronchoscope was available and views of the larynx further confirmed correct positioning of the mask.

In three cases lateral X rays of the neck were taken, which demonstrated the effectiveness of the cricoid pressure (Fig. 2(a) and (b)).

In all 10 cases, when the clamp was opened, approximately 10–15 drops of fluid dripped into the oesophagus, after which all flow ceased.

When cricoid pressure was released, in all cases the dilute barium solution immediately gushed through the drip set into the oesophagus and was subsequently observed in the pharynx when the LMA was removed. In six of the cases, the pathologist commented on the presence of white staining within the trachea.

Discussion

Intragastric pressure may increase up to 7.84 kPa in patients with an abdominal mass (such as a gravid uterus) after the administration of suxamethonium [4].

In 1961, Sellick described his method of cricoid pressure which has been adopted widely to protect the patient against passive reflux of gastric contents [5] and Wraight *et al.* subsequently showed that a force of 44 N applied to the cricoid cartilage was sufficient to protect most patients from regurgitation [6].

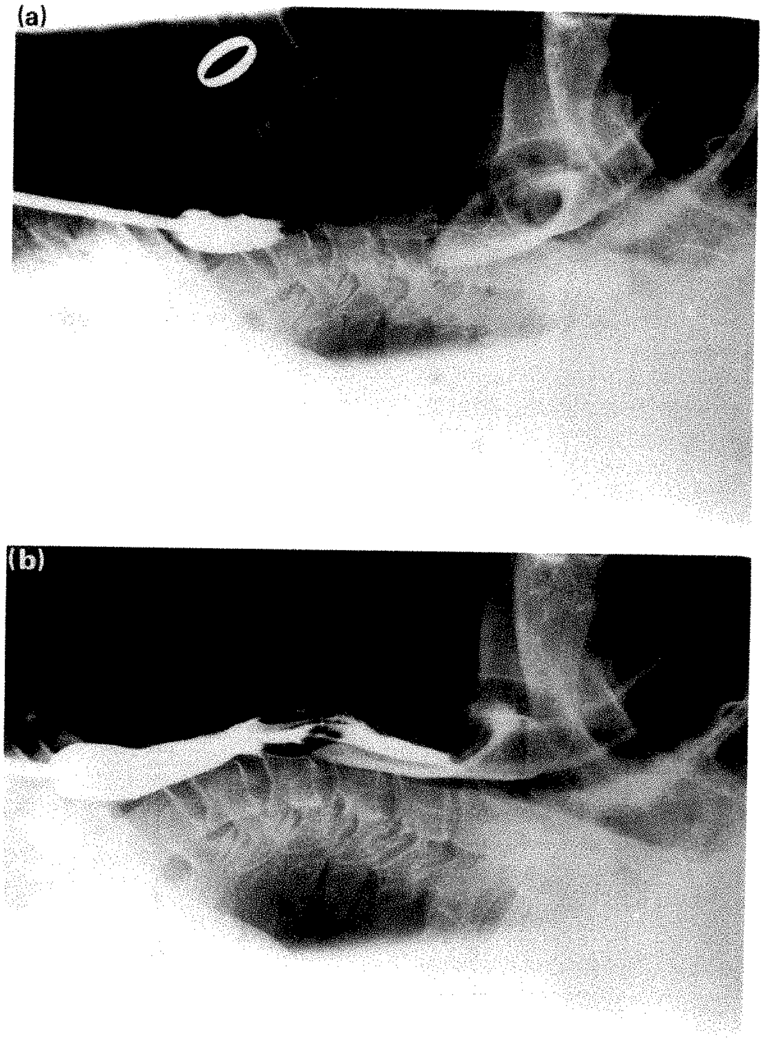

Fig. 2. Lateral X rays of the neck showing (a) cricoid pressure preventing passive reflux of barium; (b) reflux of barium when cricoid pressure was released.

The effect that the presence of the LMA has on cricoid pressure has never been examined, despite the fact that it has been used in patients at risk of regurgitation [2]. In this study, a fibreoptic bronchoscope was used to confirm that the LMA was correctly positioned, as has recently been suggested by Payne [7].

The infusion set was modified at its distal end to produce an additional lateral orifice so that flow was not obstructed by oesophageal tissue. Thus, if the flow of dilute barium into the oesophagus was prevented, it must have been as a result of the cricoid pressure alone. A weak solution of barium was used, so that regurgitated fluid in the pharynx would be clearly visible. When X rays were taken, a more concentrated solution was used.

The initial 10–15 drops of fluid that entered the oesophagus before flow ceased represented the 1 ml dead space volume in the oesophagus which had to be filled before intra-oesophageal pressures reached a level of 7.8 kPa.

The force exerted by a 4.4 kg mass in the direction of the gravitational field is 43 N, although any error in the direction of the cricoid pressure would have resulted in a cricoid force of less than 43 N.

This study therefore confirmed that a cricoid force of 43 N is protective against a distal oesophageal pressure of up to 7.8 kPa and the presence of the LMA did not prevent the cricoid pressure from being effective. However, the appearance of dilute barium in the trachea of some cadavers after release of cricoid pressure also indicates that the LMA alone does not prevent passive regurgitation.

The compliance of cadaveric tissue is reduced as a result of rigor mortis, therefore, in the more compliant tissues of live patients, it is probable that lower forces would be required to produce effective cricoid pressure.

A recent clinical study has shown that cricoid pressure does not reduce the ease of insertion or positioning of the LMA [8] and this cadaveric study suggests that the presence of the LMA does not compromise the effectiveness of cricoid pressure in preventing reflux. However, since dilute barium appeared in the tracheas of some cadavers after release of cricoid pressure, the exact rôle of the LMA in the management of failed intubation has yet to be determined.

Acknowledgments

The author thanks Dr A. Brain for the donation of two laryngeal mask airways, G. Millner (Mortuary Technician) for his assistance and co-operation, A. Lang and A. Boardman for radiographic services and Ms A. Shirley for typing this manuscript.

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Anaesthesia, 1992, Volume 47, pages 832–834

A comparison of the pharmacodynamics of rocuronium and vecuronium during halothane anaesthesia

M. G. BOOTH, B. MARSH, F. M. M. BRYDEN, E. N. ROBERTSON AND W. L. M. BAIRD

Summary

Thirty healthy patients were randomised to receive either a single bolus dose of rocuronium 0.6 mg.kg^{-1} or vecuronium 0.1 mg.kg^{-1} during halothane anaesthesia. Onset time, duration 25, duration 75 and train-of-four 70 were measured. The onset of neuromuscular blockade following rocuronium was more rapid than vecuronium ($p = 0.0001$). All other pharmacodynamic parameters were similar. During the first minute following injection of the neuromuscular blocking agent, the heart rate increased by 36% in the rocuronium group but remained stable in those patients who received vecuronium ($p = 0.0008$). No adverse effects were noted in either group.

Key words

Neuromuscular relaxants; rocuronium, vecuronium.
Anaesthetics, volatile; halothane.

A new nondepolarising neuromuscular blocking drug, rocuronium, (laboratory code, Org 9426), currently undergoing evaluation in man, is a monoquaternary aminosteroid compound, the 2-morpholino, 3-hydroxy 16N-allyl pyrrolidino analogue of vecuronium. Animal studies have shown that, when equipotent doses are compared, rocuronium has an onset of neuromuscular blockade which is twice as rapid as vecuronium, although the duration of action is similar. In these studies, the cardiovascular effects of rocuronium were, in general, slight [1], substantiated by initial clinical studies [2–8].

The neuromuscular blocking potency of rocuronium was shown to be approximately 20% that of vecuronium in anaesthetised cats and pigs [1]. In patients anaesthetised with nitrous oxide and narcotic, the ED_{90} dose of rocuronium was reported to be somewhere within the range 0.25 mg.kg^{-1} to 0.3 mg.kg^{-1} [7, 9, 10].

This study compared the pharmacodynamic profile of a single bolus dose ($2 \times ED_{90}$) of rocuronium 0.6 mg.kg^{-1} with vecuronium 0.1 mg.kg^{-1}, in 30 healthy patients anaesthetised with nitrous oxide and halothane.

Method

The prospective, randomised study was approved by the Hospital Ethics Committee. Written, informed consent was obtained from 30 healthy patients (ASA 1 or 2), aged 18 to 65 years, who were scheduled for elective nonabdominal surgery. Patients who had had anaesthesia within the previous 3 months or received medication during the past 7 days that could affect neuromuscular function were not studied. Body weight limits were imposed, calculated on the basis of [height (cm)–100] kg+25% or −15%. Additional exclusion criteria included pregnancy and those patients whose serum electrolyte and urea levels and/or liver function tests were outside normal limits.

Patients were premedicated with papaveretum and hyoscine on a body weight basis, administered intramuscularly approximately 1 h before induction of anaesthesia. Morphine was substituted for papaveretum, following the recommendation by the Committee on the Safety of Medicines (June 1991) [11]. Anaesthesia was induced with thiopentone (3–5 mg.kg^{-1}) and maintained with nitrous oxide 67% and halothane 0.5–1% (end-tidal) in oxygen. Spontaneous ventilation was retained at this stage.

Supramaximal stimuli, duration 0.2 ms and frequency 2 Hz, were delivered in a train-of-four (TOF) sequence at 10 s intervals to the ulnar nerve at the wrist via surface electrodes, and the evoked responses of the adductor pollicis were transduced and recorded by a Myograph 2000 Neuromuscular Transmission Analyser (Biometer,

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Denmark). Control responses were recorded for at least 10 min to allow stabilisation and skin temperature over the thenar eminence was monitored throughout and surface cooling minimised by application of wool gauze pads. The neuromuscular blocking drug was injected into a fast flowing intravenous infusion of 0.9% saline sited in a vein on the contralateral hand and the times were measured from completion of injection. The parameters measured were: onset (time from injection to 100% depression of the first response, T1) duration 25 (time from injection to 25% recovery of T1), duration 75 (time from injection to 75% recovery of T1), and TOF 70 (time from injection to a T4/T1 ratio of 70%).

Arterial pressure (indirect), heart rate, electrocardiograph (ECG), oxygen saturation, end-tidal CO_2 and end-tidal halothane concentration were monitored continuously throughout the study.

Patients were randomly allocated to receive rocuronium 0.6 mg.kg^{-1} (group 1: $n = 15$) or vecuronium 0.1 mg.kg^{-1} (group 2: $n = 15$). Following administration of the neuromuscular blocking drug, when the T1 response was ablated, the trachea was intubated and mechanical intermittent positive pressure ventilation (IPPV) instituted.

The demographic data from the two groups were analysed by the Wilcoxon 2 sample test, and with respect to sex, using the Chi-squared test. The pharmacodynamic and haemodynamic data were compared by the Wilcoxon 2 sample test; $p < 0.05$ was considered to be significant.

Results

The demographic data are shown in Table 1. There were no singificant differences between the two groups with regard to sex, age, body weight or height.

The pharmacodynamic data are shown in Table 2. The onset of neuromuscular block following rocuronium was 1.0 (0.2) min and 1.6 (0.5) min after vecuronium, the difference being highly significant (p = 0.0001). In all patients depression of T1 was 100%.

Duration 25 was 42.7 (11.2) min and 43.3 (6.7) min, following rocuronium and vecuronium respectively. The corresponding duration 75 measurements were 66.5 (27.7) min and 65.9 (13.6) min respectively. Duration TOF 70 was 71.2 (21.8) min and 76.6 (15.1) min in groups 1 and 2, respectively. In two patients, one in each group, the residual neuromuscular block was reversed before the TOF ratio returned to 70%, to avoid unacceptable delay in the progress of the operating list. There was no statistical difference between the recovery parameters measured in either group of patients.

The heart rate and mean arterial pressure recordings made immediately before and 1 min after injection of the neuromuscular blocking agents, but before laryngoscopy, are shown in Table 3. The mean baseline heart rates of patients in group 1 and group 2 were not statistically different.

Table 1. Mean (SD) age, weight, height and distribution of sex in the study groups.

	Study group	
	$n = 15$ Vecuronium	$n = 15$ Rocuronium
Age; years	39.9 (12.0)	40.1 (12.4)
Weight; kg	64.3 (11.7)	73.0 (7.8)
Height; cm	166.7 (6.0)	172.1 (7.8)
Females	10	5
Males	5	10

Table 2. Mean (SD) onset time of initial dose of neuromuscular blocking agent, duration 25, duration 75 and duration 0.7 in min in the study groups.

	Study group	
	$n = 15$ Vecuronium	$n = 15$ Rocuronium
Onset time	1.6 (0.5)*	1.0 (0.2)
Duration 25	43.3 (6.7)	42.7 (11.2)
Duration 75	65.9 (13.6)	66.5 (27.7)
Duration TOF 70	76.6 (15.1)	71.2 (21.8)

*Significant difference between groups p = 0.0001.

However, 1 min following injection of rocuronium the mean heart rate in group 1 patients increased, whereas in group 2, after vecuronium, the mean heart rate decreased, the difference being statistically significant (p = 0.0022). The change in heart rate, expressed as a percentage of the baseline recordings, was +36.3% (30.76) in group 1 patients and −5.5% (13.18) in group 2 (p = 0.0008).

The baseline mean arterial pressure in both groups was similar and the subsequent changes noted 1 min after injection of either neuromuscular blocking agent were not significantly different.

No untoward sequelae, such as arrhythmias or evidence of histamine release, were observed.

Discussion

This study has demonstrated that in patients anaesthetised with nitrous oxide and halothane, the onset of neuromuscular blockade following rocuronium is approximately 40% more rapid than that of vecuronium when equipotent doses ($2 \times ED_{90}$) are compared. This finding is in close agreement with work previously published [6].

However, in our study, the mean time from injection to 100% depression of twitch height (1.0 min) following rocuronium 0.6 mg.kg^{-1} was substantially faster than the onset time (1.6 min) reported by Nagashima and his colleagues, who studied the same dose [10]. Similarly, we recorded an onset time of 1.6 min following vecuronium 0.1 mg.kg^{-1} whereas other investigators, for example Rørvik *et al.* [12], have reported the onset to be 2.8 min at

Table 3. Haemodynamic data, mean (SD) in the study groups.

	Study group	
	$n = 15$ Vecuronium	$n = 15$ Rocuronium
Heart rate, baseline	64.27 (13.57)	66.47 (20.57)
Heart rate at 1 min	59.93 (12.33)*	84.47 (16.89)
% change	−5.52 (13.18)†	+36.30 (30.76)
MAP, baseline	76.73 (11.57)	82.71 (14.55)
MAP 1 min	75.27 (18.95)	86.64 (13.01)
% change	−1.97 (15.81)	+3.62 (16.00)

Significant difference between groups
*p = 0.0022;
†p = 0.0008.

the same dose level. It would seem likely that the varying results can be explained by the difference in experimental design employed in these studies. Whilst we measured the onset time of rocuronium and vecuronium when injected during steady state halothane: nitrous oxide anaesthesia, Nagashima *et al.* [10] and Rørvik *et al.* [12] recorded onset time (and recovery) during nitrous oxide: narcotic anaesthesia.

The factors which govern the onset of neuromuscular blocking drugs, other than circulation time, have not yet been fully elucidated. After undertaking extensive studies on a large number of pancuronium and vecuronium analogues, Bowman and his colleagues [13] demonstrated a clear relationship between effective dose and onset time and showed that rapid onset time, coupled with brief duration of action, could only be obtained with compounds of relatively low potency. They suggested that this could be explained, in accordance with the law of mass action, by the need for a high concentration of molecules in the biophase in order to achieve rapid receptor block. This concept has also been addressed recently by Hull [14]. If vecuronium is administered in a large dose, (with the aim of increasing the concentration of molecules in the biophase to hasten the onset of blockade), because of its inherent high drug: receptor affinity, the more rapid onset will only be achieved at the cost of very prolonged duration of action [15]. In contrast, when rocuronium is administered in approximately equipotent doses, it provides an onset of action which is substantially more rapid than vecuronium, without incurring long duration of action. This interesting pharmacodynamic profile of rocuronium, which is a compound with a potency some 6 to 8 times less than that of vecuronium, is in accordance with the hypothesis outlined above.

This study was not specifically designed to evaluate possible cardiovascular effects. However, 1 min after the injection of rocuronium, but before the stimulus of laryngoscopy and tracheal intubation, a moderate increase in heart rate was noted although the arterial pressure remained stable. The haemodynamic parameters did not change following vecuronium.

Cardiovascular effects have not been reported before in clinical studies of rocuronium. In the cat, the ratio of vagal to neuromuscular blockade was shown to be 7.2 for rocuronium and 76 for vecuronium [1]. These authors drew attention to the fact that, in this respect, vecuronium provides an especially stringent standard. However, since rocuronium is much less potent than vecuronium as a neuromuscular blocking agent, the possibility of unwanted side effects does arise. Although the increase in heart rate noted in this study was not of great clinical significance, a detailed analysis of the cardiovascular effects of rocuronium in patients, at dose levels of $2 \times ED_{90}$ and above, is warranted.

In conclusion, this study has confirmed that under halothane: nitrous oxide anaesthesia rocuronium has a significantly faster onset of neuromuscular blocking action than vecuronium when compared at dose levels of approximately $2 \times ED_{90}$. In all other respects the pharmacodynamic profile of these two compounds is similar. The possibility exists that these dose levels of rocuronium may induce a moderate increase in heart rate. Further detailed evaluation of this interesting compound is certainly indicated.

Acknowledgments

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Anaesthesia, 1992, Volume 47, pages 835–837

Unconscious learning during anaesthesia

M. JELICIC, A. DE ROODE, J. G. BOVILL AND B. BONKE

Summary

Forty-three surgical patients were, during general anaesthesia, presented (via headphones) with either statements about common facts of some years ago (group A), or new verbal associations, i.e. the names of fictitious, nonfamous people (group B). None had any recall of intra-operative events. In a postoperative test of indirect memory, patients in group A answered more questions about the 'common facts' correctly than those in group B ($p < 0.005$), which reflects the activation of pre-existing knowledge. Furthermore, patients in group B designated more 'nonfamous names' as famous (thus falsely attributing fame) than patients in group A ($p < 0.001$), which demonstrates that information-processing during anaesthesia can also take place as unconscious learning.

Key words

General anaesthesia; unconscious learning.
Memory.

There is reason to believe that some form of information-processing occurs during the state of unconsciousness induced by general anaesthesia. Studies which used indirect, or implicit, memory tests have demonstrated stimulus registration without conscious awareness during anaesthesia [1–3], though not under all circumstances [4,5]. In contrast with traditional, direct tests such as recall and recognition, tests of indirect memory do not refer to conscious recollection of a previous learning episode but bring about a change in task performance attributable to a learning period [6]. Roorda-Hrdličková and colleagues [1] were among the first to demonstrate indirect memory for neutral words presented during anaesthesia. Their findings were recently replicated and expanded [2,3].

It has been suggested that intra-operative stimulus registration reflects automatic activation of old semantic knowledge, which makes pre-existing representations temporarily more accessible in postoperative memory [7]. Almost all studies of cognition and anaesthesia employing indirect memory paradigms have involved the activation of pre-existing representations in memory. However, it cannot be denied that unconscious learning, i.e. the formation of new verbal associations in memory, also occurs in anaesthetised patients. Such indirect learning has been demonstrated, with indirect memory tests, in both normal subjects and patients with organic amnesias [8,9]. The present study was designed to investigate whether or not anaesthetised patients are capable of learning new verbal associations. The design of the study also permitted a replication of the activation paradigm.

Methods

The study was approved by the local medical ethics committee, and informed consent was obtained from adult patients (18–50 years, ASA 1–2) scheduled for strabismus surgery under standardised general anaesthesia. Patients with hearing difficulties or a history of alcohol abuse, and those who used psychoactive drugs were not studied.

The patients were randomly allocated to two groups, and the study was performed in a double-blind fashion. Pre-operative anxiety was assessed on the afternoon before surgery using the state version of the State–Trait Anxiety Inventory [10]. Immediately after induction of anaesthesia, all patients were played, through headphones, an audiotape of natural seaside sounds (waves, gulls). The headphones prevented the patients hearing sounds from the operating room and the investigators hearing the contents of the tape. Five minutes after the initial surgical incision, the seaside tape was replaced with one containing 10 repeated recordings, over 15 min. For group A, the recording comprised 10 statements about common historical facts (e.g. 'Queen Beatrix came to the throne in 1980'). A pilot study of 53 outpatients had shown that details of these selected

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common facts had largely been forgotten. For group B, the recording contained the names of 10 fictitious nonfamous people (e.g. 'Martin Petersen'). One series of the common facts on the tape for group A lasted approximately 90 s; the average duration of each statement was 6 s and the interval between statements was 3 s. For group B, one series of names lasted approximately 90 s; the average duration of each name was 1.5 s and the interval between names was 7.5 s. After administration of the experimental stimuli, the 'seaside' tape was again played to the patients for the remainder of the operation.

For all patients the anaesthetic technique used during this study was that which is common in our hospital for day-case surgery. All anaesthetics were given by one of the authors (A.D.R.). No sedative drugs were given pre-operatively. During anaesthesia the electrocardiograph was continuously monitored, as were the arterial blood pressure (noninvasively), ventilation parameters, end-tidal carbon dioxide concentration and oxygen saturation. Atropine 0.5 mg was given before induction. After pre-oxygenation for 3 min, anaesthesia was induced with alfentanil 20 μg.kg^{-1} and thiopentone 4–5 mg.kg^{-1}. When consciousness was lost, suxamethonium 1 mg.kg^{-1} was given and the trachea was intubated. Anaesthesia was maintained with 35% oxygen and 65% nitrous oxide. Additional boluses of alfentanil, 0.5–1.0 mg, were given if the heart rate or arterial blood pressure increased by more than 10% of the preoperative value. Vecuronium 4–6 mg was given for muscle relaxation, with incremental doses of 1 mg every 20 min. Ventilation was adjusted to maintain an end-tidal carbon dioxide concentration between 3.5 and 4.0%. At the end of surgery, atropine 0.5 mg and neostigmine 1 mg were given to reverse residual neuromuscular blockade, and nitrous oxide was discontinued. The trachea was extubated when patients were awake with satisfactory spontaneous ventilation. The median interval between the end of the experimental tape (common facts for group A, fictitious names for group B) and discontinuation of nitrous oxide administration was 36 min (range: 0–85 min). The minimum duration of anaesthesia was 20 min, hence some patients did not hear the 'seaside' tape again after the experimental tape. None of the experimental stimuli were administered after the nitrous oxide had been stopped.

All patients were interviewed, in the recovery room, as soon as possible after surgery. They were first asked about any recall of intra-operative events: 'What is the last thing you remember from the period before the operation?'; 'What is the first thing you remember from the period after the operation?'; 'Is there anything you remember from the period in between?'

Next, patients were given 15 questions about past events. Ten of these questions related to the statements presented intra-operatively to group A (e.g. 'When did Queen Beatrix come to the throne?') and formed the indirect memory test for activation of pre-existing memory representations.

Finally, the patients were asked to state whether each of 20 combinations of first names and surnames belonged to a famous person or not. Ten of these, making up the indirect test for the learning of new associations, were the nonfamous names presented to group B during surgery (e.g. 'Martin Petersen'). The other 10 were fillers, containing five new nonfamous names, and five new names of moderately famous people. Postoperative indirect memory for pre-existing memory representations (activation) would show up if patients from group A answered more questions about the common facts correctly than patients in group B. Indirect memory for new associations (learning) would be expressed if patients in group B designated more nonfamous names as famous than those in group A. In this case, nonfamous names (i.e. the unique combinations of first names and surnames) which lack any pre-existing memory representation, would have gained in familiarity as a result of a new memory trace (see [11, 12] for more details about this test). Data were analysed with Student's t-tests for differences between groups. A value of $p < 0.05$ was taken as significant.

Results

Twenty-five female and 18 male patients (mean age 32 years, range 18–49) were enrolled in the study. Group A consisted of 21 patients, group B of 22 patients. There were no significant differences between the groups with respect to age, gender, number of previous operations, pre-operative anxiety, duration of surgery, and interval between presentation of stimuli and testing. None of the patients had recall of any intra-operative events. Both indirect memory tests revealed evidence of information processing during anaesthesia. Mean (SEM) number of correct answers on the common facts test was 5.2 (0.46) for group A, and 3.0 (0.57) for group B ($p < 0.005$; 95% CI for true difference: 0.74–3.72). Mean (SEM) number of the 10 nonfamous names that were designated as famous on the learning test was 1.6 (0.30) for group B, and 0.3 (0.10) for group A ($p < 0.001$; 95% CI for true difference: 0.65–1.95). As a check on possible violations regarding the use of t-tests, the data were also analysed nonparametrically by Mann–Whitney's U-test corrected for ties, with similar results ($p < 0.005$ and $p < 0.0005$, for the common facts test and the famous names test, respectively). Neither for the five filler questions, nor for the filler names, was there a difference between groups that approached significance (all

Table 1. Proportions correct (for the 'common facts' test) and proportions attributed fame (for the 'famous names' test) for the two groups, for experimental and filler items.

	Group A (n = 21)	Group B (n = 22)	p
Common facts;			
Experimental	0.52	0.30	< 0.005
Fillers	0.68*	0.72*	0.59
Names;			
Experimental (nonfamous)	0.03	0.16	< 0.001
Fillers			
famous	0.90	0.88	0.74
nonfamous	0.02	0.04	0.74

*In order not to discourage patients, we selected as the five filler questions items which concerned facts that were easier to remember than the experimental ones. Thus, each patient was able to answer at least some questions correctly, hence the relatively large proportions for the fillers as compared with the proportions for the experimental facts.

Note: Group A had been administered a tape with the 10 experimental common facts, group B had heard the 10 experimental nonfamous names; p refers to p-values (t-tests for differences between means). Proportions are shown, instead of means, because the number of tested items differs between the various categories.

p-values > 0.50). Proportions correct (for the common facts test) and proportions attributed fame (for the famous names test) for both experimental and filler items are presented in Table 1.

Discussion

Our results have both theoretical and practical significance. Kihlstrom and Schacter [7] hypothesised that anaesthetised patients are able to execute some highly automated information-processing functions, but probably not the higher cognitive processing required to encode an entirely new memory trace. For this reason, indirect memory under anaesthesia was assumed to be limited to the activation of pre-existing representations in memory (see Jelicic *et al.* [13] for an extended discussion of this issue). Our results indicate that new associations may be formed in memory during anaesthesia. This suggests that some of the brain functions associated with verbal learning remain active during this state of unconsciousness, i.e. with a minimum amount of attention paid to the stimuli. Our patients did not receive any sedative drugs pre-operatively, nor were any volatile anaesthetics used in the study. This may have contributed to our findings because anaesthetics with nitrous oxide, oxygen, and opioids are known to result in a relatively high incidence of conscious awareness. This incidence diminishes with the use of volatile anaesthetics or benzodiazepines [14]. Therefore, the possibility that auditory information is transmitted to the cerebral cortex may increase when N_2O/O_2 and alfentanil are used. Furthermore, benzodiazepines, frequently used as premedicant drugs, affect performance on direct, and to a lesser amount, indirect memory tests [15]. Therefore, further studies are indicated to assess the effect of other anaesthetic techniques, including premedicant drugs and/or volatile anaesthetics. With a similar design to that used in the present study, groups of surgical patients can be tested with different anaesthetics, to be compared both among themselves, and with our results. Moreover, the demonstration that learning can take place during general anaesthesia raises the question as to what level such learning can take place.

Information processing and memory storage under anaesthesia have important implications. Inappropriate or ambiguous remarks made during surgery may lead to adverse postoperative effects. Howard [16] described two patients who had developed a post-traumatic anxiety disorder as a result of unconscious perception of negative remarks made while under anaesthesia. That quite a sophisticated form of memory storage (learning) may take place without any attention or consciousness makes clear why this can sometimes be the case.

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The influence of arm position and cardiac output on bolus clearance from the arm

A. J. McLINTIC, W. MARTIN AND A. C. TWEDDEL

Summary

The importance of arm position and cardiac output on the clearance of a bolus injection from the arm was assessed in 63 patients using technetium-99m. Injections were made in the left arm which was either adducted, abducted or adducted with the forearm flexed over the lower chest. The clearance of isotope was assessed by measuring the amount of radioactivity remaining in the arm at 10 s intervals and calculating it as a fraction of the injected dose. The clearance of Tc-99m was significantly faster and more complete from the abducted arm than from the adducted arm. There was no correlation between clearance and cardiac output.

Key words

Anaesthesia; drug clearance.
Measurement; radionuclide ventriculography.

The transit time of a bolus from an injection site in the arm to the right atrium is a major component of the arm–target circulation time. If the clearance from the arm is impaired the transit of the bolus to its target will be delayed and the latency of its effect will be increased. The aims of this study were to determine whether dynamic radionuclide imaging could be used to evaluate bolus transit from the arm to the heart and, thereafter, to assess the importance of arm position and cardiac output on the clearance of bolus injections from the arm.

Methods

Sixty-three male patients undergoing routine blood pool ventriculography using technetium-99m (Tc-99m) were studied. The study was approved by the local ethics committee and all patients gave their informed consent. An 18 gauge cannula was inserted in the cephalic vein in the upper third of the left forearm. All patients lay supine with the left arm in one of three randomly allocated positions; in group 1 adducted by the side, in group 2 abducted to 45° and in group 3 adducted with the forearm flexed over the lower chest (Fig. 1). Imaging was performed using a GE 300A mobile gamma camera with a high sensitivity, 30 cm parallel collimator and a 10° left anterior oblique (LAO) projection. This allowed simultaneous imaging of the arm and the heart. After pretreatment of the patient with stannous pyrophosphate (20 μg stannous ion per kg body weight), approximately 600 MBq of Tc-99m was diluted to 10 ml with 0.9% saline and injected over 5 s. Data acquisition commenced immediately on injection and continued for 2 min. The data were acquired into 15 2 s frames and 18 5 s frames. For calculation of cardiac output a second image was then acquired using a 30° LAO view gated to the electrocardiogram.

Analysis

Tc-99m dose. Tc-99m was prepared in 600 MBq aliquots. The decay in radioactivity from the time of preparation to the time of injection was calculated using the negative exponential equation. The precise amount of radioactivity injected was thus determined for each patient and expressed in counts per second.

Bolus clearance. Data were assimilated and analysed using a Link Maps 2000 computer. Using the computer display of stored data, a region of interest (ROI) was drawn around the venous return from the arm to the heart up to, but not including, the right atrium. The activity within the ROI was calculated in counts per second by on-board computer software and expressed as a percentage of the injected dose. This value was termed the residual arm activity (RAA). The RAA was calculated at 1 s and then at 10 s intervals after the start of injection and plotted against

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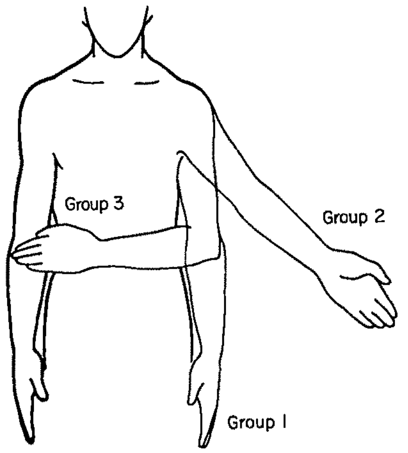

Fig. 1. Arm positions at injection.

time to form a clearance curve. To provide a summary measure of the curves for statistical comparison, the area under the curve (AUC) was calculated for each patient and divided by the length of each study (AUC/T) using the method described by Matthews and colleagues [1]. The AUC/T represents the mean RAA over the study period and is inversely related to the mean percentage of the injected dose cleared from the arm during this time [1]. A second summary measure, the RAA at 2 min, was used to reflect the magnitude and, therefore, overall rate of isotope clearance for the 2 min study period.

Cardiac output

The cardiac output was calculated from the product of left ventricular end-diastolic volume (LVEDV), ejection fraction (EF) and heart rate (HR). The LVEDV was obtained geometrically from the left ventricular long-axis and the area of the left ventricular ROI by the Dodge and Sandler method [2]. The EF was calculated by a single ROI technique in quadruplicate from the best septal blood pool ventriculogram. This technique has been fully validated in our institution [3]. The HR was derived from the mean cardiac cycle length during the acquisition of the study.

Statistical analysis

Statistical evaluation of the data was carried out using the Minitabs Release 7.2 statistical package. Data were analysed by Kruskal-Wallis, Mann-Whitney *U*-test and Spearman's Rank Correlation where appropriate. A p value of < 0.05 was considered to be significant.

Table 1. Patient details, mean (SD) or median (range). Body mass index (BMI) = weight (kg) divided by height (m). Cardiac output (Q_T, $l.min^{-1}$).

Group	Age	BMI	Q_T
1 (*n* = 19)	54	45.9	3.8
	(7.92)	(39.8–55.0)	(2.40–5.90)
2 (*n* = 17)	54	47.2	4.1
	(9.47)	(40.6–52.8)	(1.12–5.79)
3 (*n* = 17)	50	48.3	4.5
	(8.79)	(37.7–56.1)	(2.99–8.80)

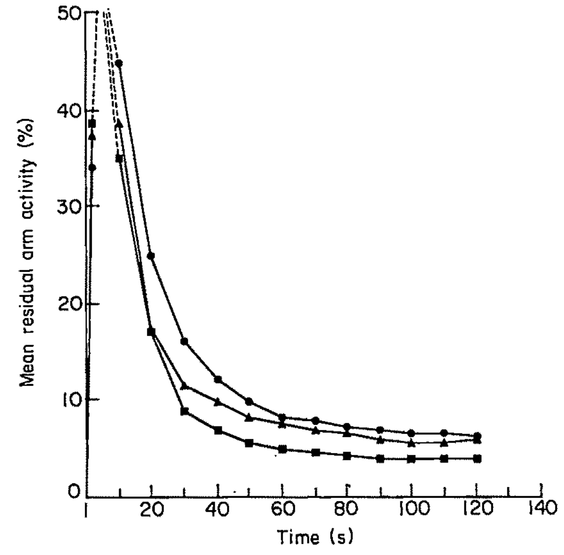

Fig. 2. Clearance of Tc-99m from arm: decline in mean residual arm activity with time for each group. ●, group 1; ■, group 2; ▲, group 3. Injection commenced at Time 0 s. AUC/T (area under the curve divided by time) calculated for time period 10 to 120 s.

Results

Images from 10 patients could not be analysed because visualisation of the arm was not complete. Data were available from 19 patients in group 1 (arm adducted), 17 in group 2 (arm abducted) and 17 in group 3 (arm adducted with forearm flexed). There was no difference between the groups in terms of mean age, body mass index or cardiac output (Table 1). The RAAs between 1 and 10 s could not be determined accurately because the initial emission of radioactivity from the full 600 MBq bolus exceeded the upper limit at which the gamma camera's response is linear. The clearance curves from 10 s on, however, clearly illustrate the difference in the clearance patterns of the three groups, with group 2 having a more rapid clearance of isotope than group 1, and group 3 intermediate (Fig. 2). Statistical comparison of the curve summary measures (AUC/T and 2 min RAA) confirmed the differences. The AUC/T of group 1 was significantly greater than that of group 2. Group 3 was intermediate between groups 1 and 2, but was not significantly different from either (Table 2). The 2 min RAA of group 1 was significantly larger than that of group 2. Group 3 results were again intermediate and not significantly different (Table 2). Thirteen patients

Table 2. Estimations of clearance; mean, median (range). Area under the curve standardised for time (AUC/T). *Significantly different from group 2.

Group	AUC/T (%)	2 min residual arm activity (%)	2 min residual arm activity. Number of patients with:	
			> 5%	> 10%
1	14.05, 13.22*	6.32, 5.35*	13	3
	(6.74–22.42)	(2.54–12.66)		
2	9.94, 10.33	3.81, 3.38	4	0
	(3.37–18.02)	(1.82–6.34)		
3	12.02, 10.38	5.46, 4.23	5	2
	(6.08–29.62)	(2.87–17.72)		
p	0.019	0.003		

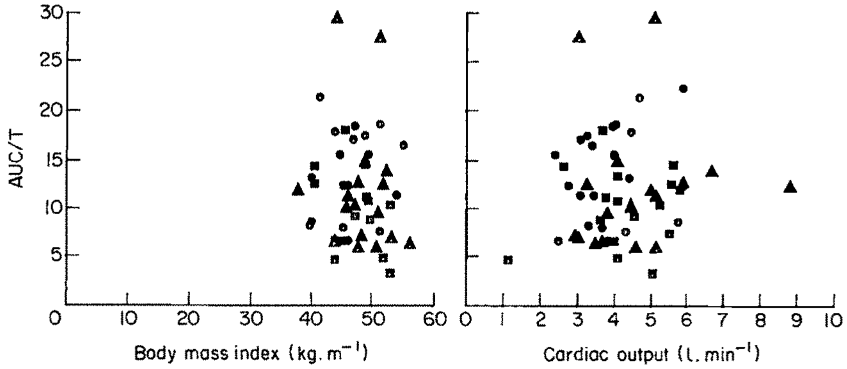

Fig. 3. Relationship between AUC/T (area under the curve divided by time), body mass index and cardiac output. ●, group 1; ■, group 2; ▲, group 3.

in group 1 had a 2 min RAA of more than 5% and three more than 10% compared with four and zero in group 2, and five and two in group 3 (Table 2). Cardiac output is plotted against AUC/T in Figure 3. There was no significant correlation between CO and AUC/T either in the population as a whole or within each group. Body mass index (BMI) is plotted against AUC/T in Figure 3. Again, there was no significant correlation between the two.

A frequent observation in group 1 scans was areas of isotope 'hold-up' within the axilla and the antecubital fossa (Fig. 4). Isotope pooling was less common in group 3 and was never seen in group 2.

Discussion

The clearance of a bolus injection from the arm can be readily assessed using dynamic Tc-99m imaging. The technique is dependent on complete 'visualisation' of the entire path of the bolus from injection site to the heart. For this reason, a large collimator is essential and the cannulae must be sited in a proximal position in the left arm. Pretreatment with stannous pyrophosphate results in the Tc-99m being bound to red blood cells (RBC) and allows the blood pool within the heart and venous return to be identified and outlined. In addition, as the Tc-99m is rapidly and almost completely bound to RBCs there is little radioisotope lost to the extravascular space and the clearance of radioactivity from a ROI becomes dependent on the blood flow from that region [4]. As Tc-99m has a half-life of 6 h, natural decay in radioactivity will have had no significant bearing on the results from the 2 min study period.

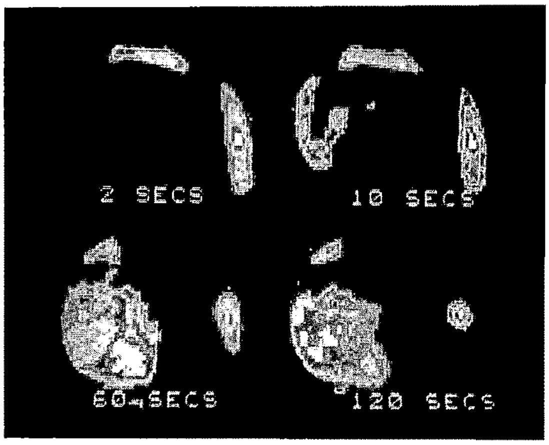

Fig. 4. Bolus clearance from an adducted arm: left anterior oblique image from Tc-99m scan of left arm and heart. At 2 s bolus has filled left arm and approaches right atrium; at 10 s bolus passing through right heart and filling pulmonary vasculature; at 60 s, right and left heart fully visualised but pool of Tc-99m remains in upper arm. At 120 s, pool of Tc-99m still present at axilla.

The lack of correlation between bolus clearance and cardiac output was surprising as the venous return to the heart and cardiac output are interdependent. It may be, however, that the influence of cardiac output on venous blood flow varies between individual venous systems and may be reduced by local factors. These may include impedance from soft tissue, the tortuosity of the vein's course and gravity.

The clearance of the bolus injection from the arm was significantly influenced by the position of the arm at injection. When the arm was adducted the clearance of isotope was significantly slower than when the arm was abducted. It is well recognised that the passage of catheters along the infraclavicular portion of the cephalic vein can be impeded by both an axillary valve and the acute angle taken by the cephalic vein as it pierces the clavipectoral fascia [5]. This angle will be more acute when the arm is adducted and may well be the cause of the isotope 'hold-up' which was seen in the axilla. An obstruction at this point would also affect distal flow and account for the pooling which was seen within the complex of veins in the antecubital fossa.

The significance of arm position on bolus transit has not been assessed in the clinical setting but there are several areas where it may be of considerable importance. Because of hold-up and delayed transit, drugs given into an adducted arm are likely to have a longer latency of effect than those given into an abducted arm. This should be remembered whenever a bolus effect is required, particularly in anaesthesia where a short onset of action is critical to both the safety of a rapid sequence induction technique and the accuracy of dose–effect titrations. A drug which is pooled in the arm also has the potential for mixing and precipitating with subsequent incompatible agents to produce an apparent adverse drug reaction.

In group 3, although the mean values tended to lie between those of the other two groups, there was considerable interpatient variability. Indeed, group 3 contained the patients with the slowest clearance in the study with one having a 2 min residual arm activity of over 17% of the injected dose. The wide range in 2 min values was also present in group 1, and highlights the unpredictable nature of bolus clearance from adducted arms. This may have particular relevance in the research setting where the consistency of a dose–effect relationship may well be compromised if drugs are administered via an adducted arm.

The importance of our findings will vary depending on the clinical situation. On the one hand, differences in bolus clearance are likely to be reduced by administering drugs through fast running infusions. On the other, the importance of arm position may well increase when smaller bolus volumes are used and in circumstances where blood flow is already compromised, such as in the elderly or hypovolaemic patient. Whatever the setting, however, we would suggest that drug hold-up in an adducted arm should always be considered if there is an unexpected delay in the onset of action of an intravenous bolus.

Acknowledgment

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Anaesthesia, 1992, Volume 47, pages 842–844

Cannulation of the internal jugular vein

The very high approach

F. M. MESSAHEL AND A. A. AL-MAZROA

Summary

A new approach to internal jugular vein catheterisation in the neck (the 'very high' approach) was used in 335 patients over a 12-month period. The success rate was 100% and there were no complications. It proved to be an easy technique to learn and may be particularly useful in difficult and emergency situations.

Key words

Veins; cannulation, internal jugular.

Cannulation of large central veins is most commonly performed using either the internal jugular or the subclavian vein. However, the insertion of central venous lines is not without hazard and carries the potential for serious complications [1–9]. The occurrence of these complications has been the stimulus for the continuing search for safer routes of access.

In the neck, the carotid triangle (Fig. 1) is limited posteriorly by the sternocleidomastoid muscle, anteriorly and inferiorly by the omohyoid muscle and superiorly by the stylohyoid and posterior belly of the digastric muscles. In the nonobese neck, the carotid triangle is usually an obvious surface feature, presenting as a relatively small triangular depression, best seen with the head rotated to the other side [10]. In this position the internal jugular vein is almost a subcutaneous structure, only separated from the skin by fascia and the platysma muscular sheet. The carotid triangle contains the common carotid artery and its bifurcation into internal and external carotid arteries. In this triangular space the internal jugular vein lies lateral to the internal carotid artery.

It would seem that cannulating the internal jugular vein at this 'very high' level might have several advantages and might have a low complication rate. To confirm these theoretical advantages, a study of its use in a number of patients was performed.

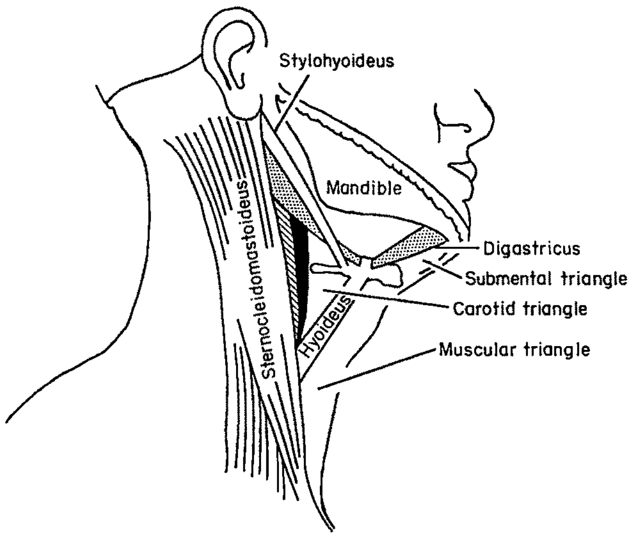

Fig. 1. Anatomy of the carotid triangle; ▨, internal jugular vein; ■, carotid artery.

Method

Adult patients on scheduled surgical operating lists and patients admitted to the intensive care unit in whom central venous cannulation was routinely indicated as part of their haemodynamic management were included in the study. Those patients who needed prolonged total parenteral nutrition were excluded. All cannulations were performed using the right internal jugular vein.

Patients were prepared as for other procedures of internal jugular vein cannulation [1]. With the patient's head turned to the left side, the anatomical carotid triangle

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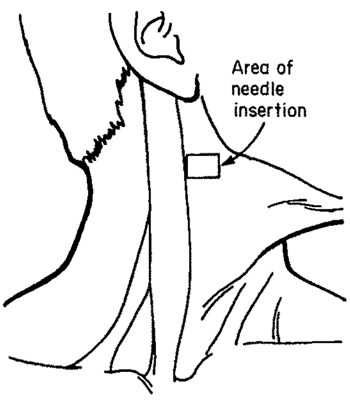

Fig. 2. Site of needle insertion.

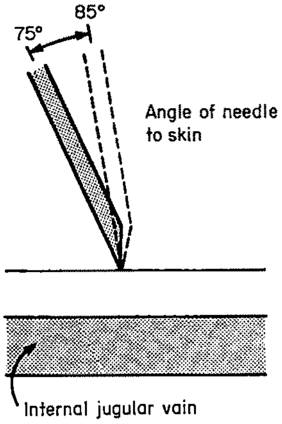

Fig. 3. Angle of needle during insertion.

was identified and the internal carotid artery was located by palpation with the tips of the index and middle fingers. A point lateral to the artery as high as practicable below the angle of the mandible was chosen for skin puncture (Fig. 2). Lignocaine 1% was infiltrated intradermally and a 2 mm skin incision made with the tip of a pointed scalpel. Through this incision, the tip of the introducing needle (attached to a 5 ml syringe) was passed in a caudad direction. The needle was adjusted during insertion so that an angle of 75–85° to the coronal plane was obtained (Fig. 3). A negative pressure was maintained on the syringe while the needle was slowly but firmly advanced until venous blood was freely aspirated. The Seldinger technique [11] was then used to place the venous catheter. If difficulty was encountered in passing the guidewire, the angle of the needle to the skin was reduced until there was easy passage. Once inserted, the catheter was attached to an extension tube which was looped round the pinna of the ear. The whole area was covered with a transparent dressing ('Op-Site', Smith and Nephew) which was split to avoid covering the ear. A chest X ray was then taken to confirm catheter tip position.

Results

The study lasted for a period of 12 months. There were 335 patients in whom internal jugular venous cannulation was performed using the 'very high' approach. The age range was 12–91 years (mean 38.7). On the first attempt internal jugular venepuncture was successful in 286 (85.4%) patients; the remainder were successful after a second attempt through the same skin puncture.

The point of skin puncture was found to be at a distance of 1–1.5 cm from the angle of the mandible. When the needle was introduced, internal jugular venepuncture occurred at a distance between 0.5 and 1 cm from the surface of the skin. All catheters were removed between 1 and 11 days (average 3.8 days) after insertion and there were no observed complications during this period.

Discussion

The absence of any major complications (e.g. pneumothorax, puncture of a major vessel inside the thorax, injury to nerves) using this approach to the internal jugular vein confirmed the theoretical advantage. The most probable reasons for this were the high site of venepuncture in the neck, the angle of insertion of the needle and the superficial position of the internal jugular vein in the carotid triangle. The approach also proved to be very simple for trainees to learn.

On the chest X ray, in the average-sized individual, when the catheter was inserted 15 cm, the tip was found to be either in the brachiocephalic vein or lower down in the upper part of the superior vena cava. Adjustment of the intravascular part of the catheter had to be made in patients with either a long or a short neck. The absence of any arrhythmias during the procedure was probably due to the very high venepuncture avoiding irritation of the myocardium.

Surgery (other than on the head and neck) once started could continue unhindered when cannulation of the internal jugular vein was performed using this approach and the temporary imposition of a 15° head-down tilt was acceptable to the surgeon.

Contrary to other approaches for internal jugular vein catheterisation, conscious patients were able to move their neck freely while the catheter was in place. This could be because of lack of pain at the site of insertion as there was no intramuscular penetration by the introducing needle.

This study has shown that the 'very high' approach carries many advantages over the 13 other approaches described for the cervical insertion of internal jugular vein catheters: the high [12, 13], middle [14], low [15], anterior [13] and posterior [16]. The very high approach is an addition to them but its ease of use and lack of complications may make many of these other approaches obsolete.

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Anaesthesia, 1992, Volume 47, pages 845–848

Six months of shivering in a district general hospital

A. W. A. CROSSLEY

Summary

Of 2595 patients admitted to a recovery room in Derbyshire Royal Infirmary over a 6-month period, 164 (6.3%) shivered postoperatively. Data regarding the anaesthetic techniques to which these patients had been subjected were gathered from the Derby Anaesthetic Audit System. Subsequent analysis demonstrated the importance of a number of factors that led to shivering, including male gender, anaesthetic techniques involving spontaneous ventilation, and anticholinergic premedication. The administration of pethidine, alfentanil or morphine intra-operatively reduced the incidence of shivering postoperatively.

Key words

Anaesthesia.
Complications; shivering.

The reported incidence of shivering following general anaesthesia varies between 5 and 65% [1]. Whilst many patients who shiver complain of feeling cold, and shivering may be associated with low core temperatures, its occurrence is unpredictable and it may occur without change in core temperature [2–4]. Oxygen consumption may rise dramatically during shivering in the recovery period with a concomitant increase in cardiac output, hypoxaemia, elevated arterial carbon dioxide tension and lactic acidosis [5–7]. The tendency to hypoxaemia may be accentuated by other factors during the recovery period, such as periods of respiratory depression or obstruction and the excretion of nitrous oxide.

This paper presents data collected from our audit system over a 6-month period concerning patients who entered one recovery room in Derbyshire Royal Infirmary and who subsequently shivered. It aims to disclose some features of the aetiology of shivering after general anaesthesia.

Methods

Data regarding 164 patients who shivered in one recovery area during the 6-month period from 1 July to 31 December 1990 were gathered by the recovery room staff. The recovery room, a seven-bed unit, provides recovery facilities for four operating theatres serving the surgical specialties of otorhinolaryngology, oromaxillary surgery, orthopaedics and general surgery. The majority of the orthopaedic surgery relates to trauma. Occasional work for other specialties takes place as part of the emergency commitment. Shivering was defined as visible tremor involving the head, neck, shoulders and extremities, or generalised and visible shaking resembling normal thermogenic shivering. One patient who developed rigors in association with a blood transfusion 3 h after operation was not included. The data recorded included the total duration and number of episodes of shivering, and an attempt at classification of the degree of shivering as mild, moderate or severe. The classification of shivering was noted during the study to be prone to considerable observer error and has not been analysed further. Details of the anaesthetic technique administered to all the patients who entered the recovery room during the study period were obtained from the Derby Anaesthetic Audit System, which has been described elsewhere [8].

Data were analysed using the SPSS-PC statistical package, by Chi-squared tests, Student's *t*-test or linear regression analysis where appropriate. Logistic regression analysis was performed to identify the influence of individual factors upon the outcome of peri-operative shivering. This technique builds a regression equation that can be used to predict the outcome, in this case peri-operative shivering. The variables were recoded as indicator variables that recorded the presence or absence of each component. The mode of ventilation and the muscle relaxant used were combined into a new variable that represented ventilatory technique. Similarly, the identity of the anaesthetists involved were used to construct a variable that represented

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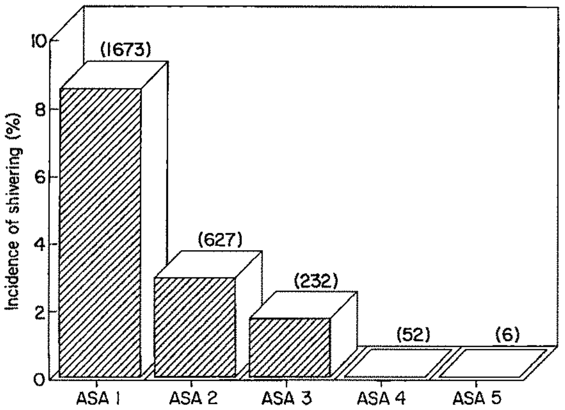

Fig. 1. The incidence of shivering by ASA category. The bars represent the percentage of patients in each ASA category who shivered postoperatively. The number in brackets above each bar is the total number of patients in each category.

the seniority of the most senior anaesthetist present during the procedure. Age was recorded in years, and the duration of each case was recorded in minutes. Cases recorded as lasting longer than 6 h were removed from the analysis. Cases with missing data elements were also removed from the analysis, and the regression equation was generated by backwards stepwise elimination of variables. The best fitting model was achieved when the analysis was confined to elective patients who received general anaesthesia that involved volatile agents. The model χ^2 in this circumstance was 615.341 ($p < 0.0001$) and the goodness of fit statistic was 46.79 ($p = 0.48$), indicating a good fit of the data to the model. This model correctly predicted shivering in 77.8% of cases.

Results

During the 6 month period of the study, 2595 patients were admitted to the recovery room. Of these, 693 had undergone emergency surgery. The remainder were elective operations, of which 80 were day cases. One hundred and twenty-four procedures were performed under regional anaesthesia. The remaining 2471 patients received general anaesthesia.

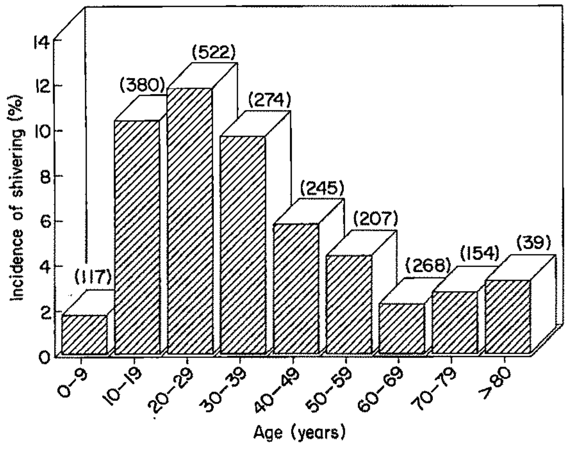

Fig. 2. The incidence of shivering by age. The bars represent the percentage of patients in each age group who shivered postoperatively. The number in brackets above each bar is the total number of patients in each group.

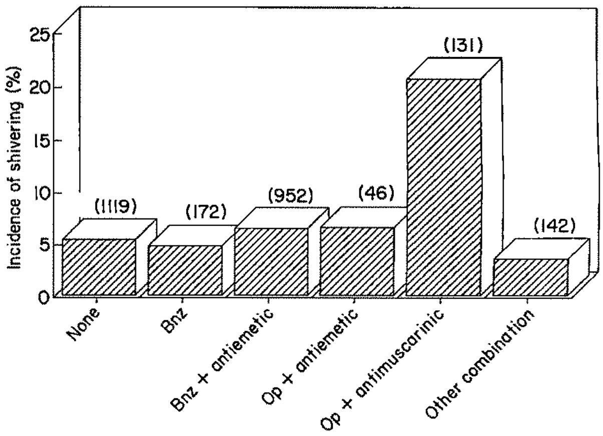

Fig. 3. The incidence of shivering by premedication group. The bars represent the percentage of patients in each group who shivered postoperatively. The number in brackets above each bar is the total number of patients in each group. Bnz, Benzodiazepine, Op, Opioid.

Postoperative shivering occurred in 164 patients (6.3%). Shivering occurred in 106 of 1370 males (7.7%) but in only 58 of 1225 females (4.7%). The proportion of patients who shivered was higher in elective patients (7.2%) than in emergences (3.8%). This may reflect the different case types in the emergency group. Shivering was commoner in ASA 1 patients than in other ASA categories (Fig. 1) and was commoner in young adults than in children or the elderly (Fig. 2). Of the 2471 patients who received general anaesthesia, 2398 were given volatile agents. Seventy-three patients who received general anaesthesia that did not involve volatile agents did not shiver subsequently.

Data regarding the length of the operative procedure were incomplete or missing in 79 patients. In the remaining 2516 patients, the mean (SD) duration of operation in patients who subsequently shivered was 73.9 (50.6) min ($n = 160$) and 63.9 (53.9) min ($n = 2356$) in those who did not. This difference was statistically significant ($p < 0.05$). The overall incidence of shivering in this sample is 6.3%, as in the whole study, and the sex ratio, ASA distribution and age distribution are also the same.

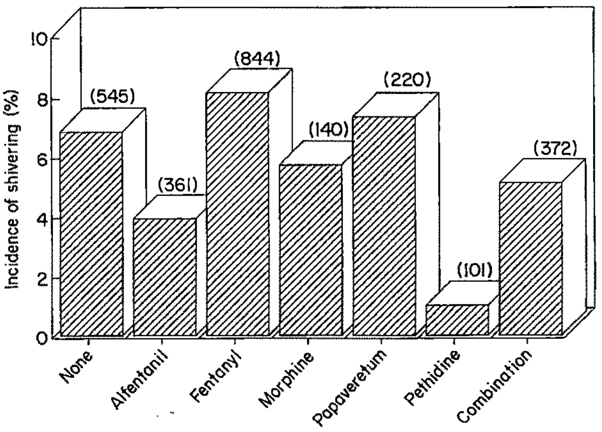

Fig. 4. The incidence of shivering in relation to intra-operative administration of opioids. The bars represent the percentage of patients in each category who shivered postoperatively. The number in brackets above each bar is the total number of patients in each category.

Table 1. Logistic regression analysis.

	Coefficient	p
Duration of procedure	0.0062	0.0002
Enflurane administration	0.3159	0.0181
Male gender	0.6200	< 0.0001
Premedication		
Antiemetic	0.6382	0.0101
Anticholinergic	1.5099	0.0020
Benzodiazepine	10.7062	0.1667
None	10.9516	0.1576
Anaesthetic technique		
Spontaneous ventilation		
without relaxant	0.6735	0.0004
after suxamethonium alone	1.1406	< 0.0001
after suxamethonium and a competitive relaxant	1.3699	< 0.0001
ASA status		
ASA 1	1.5207	0.0001
ASA 2	0.7587	0.0380
Procedure		
General surgery	1.3022	0.0008
Orthopaedic surgery	1.3199	< 0.0001
Fluid administration		
Crystalloid	0.4429	0.0462
Blood	1.9419	< 0.0001
Age	−0.0348	< 0.0001
Elective surgery	−0.5841	0.0702
ENT surgery	−0.4666	0.0174
Propofol administration	−0.6272	0.0001
Opioid administration		
Alfentanil	−1.1533	< 0.0001
Morphine	−1.1779	< 0.0001
Pethidine	−8.8999	0.2207
Regression equation constant	−9.3782	0.2232

A total of 1121 patients received no premedication and, of these, 59 (5.3%) subsequently shivered; 1474 patients were premedicated, of whom 105 (7.1%) shivered. This difference is not statistically significant. However, in patients who received a premedicant, there was a marked effect of that premedicant upon the incidence of postoperative shivering (Fig. 3), in that the incidence of shivering was higher in patients who received an anticholinergic premedication.

The administration of intra-operative opioid also influenced postoperative shivering (Fig. 4); shivering was less frequent in patients who received alfentanil or pethidine. This observation is compatible with previous reports that pethidine may stop postoperative shivering [6, 9–11] and with the clinical impression that alfentanil has a similar effect. There was no apparent effect of induction agent or of intravenous fluid administration on the incidence of postoperative shivering.

In 1178 patients, the anaesthetic technique included spontaneous ventilation. Of these, 108 (9.1%) patients shivered postoperatively, compared with 56 of 1293 patients (4.3%) in whom the anaesthetic technique included intermittent positive pressure ventilation (IPPV). The choice of muscle relaxant did not influence the incidence of shivering.

Logistic regression analysis was undertaken to determine how well the data collected predicted the occurrence of postoperative shivering. The logistic regression coefficients generated are shown in Table 1, together with their significance values. This method of analysis tests the null hypothesis that the coefficient is significantly different from zero. The logistic regression analysis confirmed the influence of gender, age, duration of procedure and ASA status upon the occurrence of shivering postoperatively. The analysis also confirmed the influence of techniques involving spontaneous ventilation. In addition, it suggested that the administration of crystalloids and of blood have a small but significant effect, and increase the incidence of shivering. Similarly, it confirmed the influence of anticholinergic premedication, and suggested that there is a small but significant effect of antiemetic premedication, which increases the incidence of shivering.

The logistic regression analysis also confirmed the effectiveness of intra-operative administration of alfentanil in reducing shivering, and suggested that morphine has a similar effect. The use of propofol for induction reduced postoperative shivering. The identity of the anaesthetist, his or her seniority, the remaining induction agents and opioids and the identity of the volatile agent with the exception of enflurane were found to have no significant influence on postoperative shivering.

The mean (SD) axillary temperature in patients who shivered was 36.2 (0.7)°C ($n = 164$). The range of duration of each shivering episode was 10 s to 45 min of continuous shivering. However, the majority of episodes were short, and the modal duration of each episode of shivering was 59 s. In 62.3% of the patients, the duration of each episode was 5 min or less. The range of number of episodes was from 1 to 73. The modal number of episodes of shivering was 1; 74.6% of the group had four or less episodes of shivering.

The data collected could not be used to determine the effect of body temperature on the incidence of shivering, because the temperature data for those who did not shiver were incomplete. However, there was a wide range of axillary temperatures among patients who shivered, and there was no correlation between axillary temperature and the number of episodes of shivering ($r = 0.03$), the duration of each episode of shivering ($r = -0.14$) or the total time spent shivering ($r = -0.16$).

Discussion

The occurrence of a syndrome characterised by involuntary movements resembling those of thermogenic shivering after general anaesthesia has been recognised for many years. The phenomenon resembles true thermogenic shivering in a number of ways, in that the involuntary movements are often accompanied by peripheral vasoconstriction and piloerection. The aetiology of this phenomenon remains unclear.

Perhaps the most confusing aspect is whether the phenomenon is truly one of thermogenic shivering, and therefore related to heat loss under anaesthesia, or whether it is a neurological abnormality related to recovery from anaesthesia. The answer to this question lies at the heart of rational treatment of the phenomenon. A number of studies [2–4] have failed to demonstrate a correlation between the occurrence of postoperative shivering and body temperature, usually measured in the axilla. The present study was unable to determine the relationship between axillary temperature and the occurrence of shivering, but there was a wide variation in axillary temperature in those who shivered. Over half of those who shivered had an axillary temperature greater than 36°C and would normally be considered to be normothermic. However, this cannot be taken as an indication of the degree of heat loss in these individuals, because total body heat was not measured either before or after surgery. If the phenomenon is truly one of thermogenic shivering, then the stimulus to shiver is presumably a reflection of total heat loss, and this may correlate poorly with the axillary temperature.

The role played by anaesthetic technique in initiating this phenomenon is clearer. The present study showed that postoperative shivering occurs predominantly in fit, healthy, young males subjected to anaesthetic techniques involving spontaneous ventilation and volatile agents. The incidence of shivering in this subgroup was 10.5%, as compared with 6.3% for the study overall, and 7.5% for a similar group of women, regardless of premedication or intra-operative opioid administration. Patients who did not receive a volatile agent did not shiver subsequently. No patient who received a regional anaesthetic technique shivered, even though shivering occurs following epidural anaesthesia in other situations [12, 13].

It was an unexpected finding that the administration of an anticholinergic premedication increased the probability of shivering postoperatively. The logistic regression analysis suggests that antiemetic premedication also increases the probability of shivering. The effect of intra-operative opioid administration was expected from the published literature. Pethidine has been shown to be effective in stopping postoperative shivering in a number of studies [9–11] and in the present study only one of 101 patients given pethidine intra-operatively shivered postoperatively. The logistic regression coefficient for pethidine proved not to be significantly different from zero, possibly because of the small number in this group. Anecdotal evidence suggested that alfentanil was equally effective although somewhat shorter in duration of action, and this observation is supported by the current study. In addition, the logistic regression analysis suggested that morphine has a small but significant effect, and this observation has been reported only once before [14]. In contrast, Pauca *et al.* [11] found that morphine given in incremental doses postoperatively was no better than saline in terms of its efficacy against shivering. Controlled prospective studies are now required to confirm the efficacy of alfentanil and morphine, and to investigate the effects of anticholinergic and antiemetic premedication.

The bulk of the data presented in this study was derived from the Derby Anaesthetic Audit System [8], which allows the collection of a large amount of sequential information over a long period of time. However, this system is not without its problems. Being a paper-based system, it is liable to marking and transcription errors. The system has not been subjected to scientific evaluation, and the data set collected is not comprehensive enough to allow in-depth analysis of many of the phenomena in which we would be interested. In particular, it collects very little outcome data in its present form, which necessitated the collection of the recovery room data separately in this study. However, the system is capable of identifying the anaesthetic techniques used in individual patients, and may therefore be used to select particular groups for further data verification and study.

The present study has highlighted a number of areas for further study. Postoperative shivering causes considerable discomfort and distress for a significant proportion of patients during recovery from anaesthesia. A deeper understanding of the aetiology and physiology of postoperative shivering may enable a more rational treatment to be brought to bear upon the problem.

Acknowledgments

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The laryngeal mask airway in infants

A. MIZUSHIMA, G. J. WARDALL AND D. L. SIMPSON

Summary

Clinical and fibreoptic assessment of positioning of the size 1 laryngeal mask airway was performed in 50 infants. A clinically patent airway was obtained in 47 patients at the first attempt, but perfect positioning, as assessed by fibreoptic laryngoscopy, was found in only 22 instances. Despite an airway initially patent, delayed airway obstruction occurred in 12 infants. It is concluded that clinical airway patency does not guarantee ideal positioning of LMA in infants, and that care should be taken to ensure continued airway patency because of the tendency of the LMA position to deteriorate in this group of children.

Key words

Anaesthesia; paediatric.
Age factors; infant.
Equipment; laryngeal mask airway, fibreoptic laryngoscope.

Several recent studies have considered the use of the laryngeal mask airway (LMA) in children [1–4], but none as yet has focused upon its use in infancy [5]. It is in this group of very young children that the relative anatomy of the upper airway differs most significantly from that of the adult [6], and thus difficulties with insertion and positioning of the LMA might be expected to occur more frequently. We therefore assessed the use of the LMA in infants, using a fibreoptic laryngoscope.

Methods

Observations were made on 50 consecutive ASA 1 infants in the first year of life, undergoing elective minor surgery (general and plastic) as inpatients or day cases. Patients who were not fasted or who required intermittent positive pressure ventilation were not studied.

A standardised anaesthetic technique was used with no premedication. Anaesthesia was induced and maintained with halothane in nitrous oxide (50–67%) and oxygen, the patients breathing spontaneously through a Jackson-Rees modified Ayre's T-piece system. Electrocardiogram and arterial oxygen saturation ($Sp\text{O}_2$) by pulse oximetry (Nellcor N-100) were monitored continuously from induction.

LMAs were inserted when anaesthesia was judged to be sufficiently deep by members of the anaesthetic department, all of whom had previous experience of the technique in children. For all patients, regardless of weight, a size 1 LMA was inserted in one of two ways: either in the standard fashion, according to the manufacturer's instructions [7], or in reverse, with the distal opening initially facing the roof of the mouth, turning the LMA through 180° on reaching the posterior pharyngeal wall [8]. The method of insertion used depended upon the preference of the individual anaesthetist. Once the LMA was inserted, the cuff was inflated with 2–4 ml air.

Correct insertion was determined by resistance to continued advancement of the LMA, by forward bulging of the larynx during insertion, and by a small amount of outward movement of the LMA on cuff inflation. Clinical airway patency was then confirmed by observing synchronous respiratory movements of the chest and reservoir bag, by a lack of indrawing in the intercostal and supraclavicular spaces, and by noting air entry in both axillae on ansuculation when gently inflating the lungs. The minimum value of $Sp\text{O}_2$ during insertion and 3 min thereafter was noted.

The actual positioning of the LMA was ascertained by fibreoptic laryngoscopy (Olympus ENF-P2) while an assistant prevented the LMA from dislocation. Laryngoscopic findings were classified as shown in Table 1 [4].

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Table 1. Classification of laryngoscopic findings.

I: glottis only seen
II: epiglottis and glottis seen
III: epiglottis impinging on grille, glottis seen
IV: epiglottis downfolded, glottis not seen

Table 3. Delayed clinical airway obstruction (n = 12).

Body weight: up to 6.5 kg	5	12
6.6–10 kg	7	
Technique of LMA insertion: standard	5	12
reverse	7	
Laryngoscopic finding at LMA insertion: I	6	12
II	1	
III	4	
IV	1	
Minimun $S\mathrm{po}_2$ at LMA insertion: 100–95%	9	12
94–90%	1	
89–85%	2	
Minimum $S\mathrm{po}_2$ at airway obstruction: 100–95%	3	12
94–90%	5	
89–85%	4	
Probable cause: transfer	5	12
position change	1	
copious secretions	1	
uncertain	5	
Treatment: jaw suport	7	12
face mask	4	
tracheal intubation	1	

Clinical and fibrescopic airway patency was assessed by one of two observers. Depending on the clinical patency, the LMA was either taped in position or re-inserted. Clinical observation was continued until the end of anaesthesia.

Results

There were 37 males and 13 female infants, aged from 3–52 weeks and 3.8–10.0 kg. The LMAs were inserted by 12 anaesthetists: four consultants, three senior registrars, three registrars, and two senior house officers.

After first insertion, a patent airway was observed in 47 cases. Second and third attempts were required, in two and one cases respectively, in order to obtain a patent airway. In one of the three cases, laryngospasm developed following the first insertion, but the LMA was satisfactorily re-inserted at a deeper plane of anaesthesia.

Once an airway was clinically patent only four patients developed an $S\mathrm{po}_2$ of less than 90% (lowest 85%) within 3 min thereafter. All of these patients responded to temporary hyperventilation, and $S\mathrm{po}_2$ was always above 95% when laryngoscopy was performed.

Table 2 summarises the findings of fibreoptic laryngoscopy, which was performed after confirming a clinically patent airway. Perfect positioning of the LMA (grade I) was observed in only 44% of all cases. Two groups, subdivided by body weight into those above or below 6.5 kg, showed no difference in the incidence of fibreoptic grade I. Reverse insertion gave a marginally higher incidence of grade I than standard insertion, 47% and 40% respectively. Kinking of the LMA was not observed in any case. There was no correlation between any of the following factors; laryngoscopic findings, body weight, insertion technique, and minimum $S\mathrm{po}_2$.

Although a patent airway was secured initially, complete or partial airway obstruction developed in 12 cases, either in the anaesthetic room or operating room, as summarised in Table 3. The incidence of delayed airway obstruction was unrelated to weight, insertion technique, fibreoptic grade, or minimum $S\mathrm{po}_2$ within 3 min of insertion. In three cases, fibreoscopy was repeated, and a deterioration in LMA position was noted (two cases from grade I to II and one from III to IV). Of the 12 cases of delayed obstruction, seven responded to minor adjustments of the jaw or the LMA, but in the remainder, the LMA was removed and facemask anaesthesia or tracheal intubation employed. Patient movement was particularly associated with deterioration in LMA position.

Discussion

Previous studies of the LMA in children of all ages have demonstrated a high incidence of clinical airway patency after the first attempt at insertion [1–5]. We confirmed this finding in infants, achieving a successful first insertion rate of 94%, suggesting that insertion of the LMA is not more difficult in this age group.

The LMA was inserted in one of two ways. Subsequent analysis of our data revealed no difference in the incidence of the various fibreoptic grades, the incidence of minimum $S\mathrm{po}_2$ or of clinical survey obstruction, between patients having the masks inserted in the standard or reverse fashion. It is suggested that the reverse method can be used as an effective alternative technique to negotiate the posterior pharynx in infants [8].

We chose to use a size 1 LMA for all the infants, which is at variance with the manufacturer's recommendations that a size 2 LMA be employed for patients weighing over 6.5 kg. In a previous study, we observed that the size 2 was rather bulky and difficult to insert in this age group, and that the size 1 was a more satisfactory alternative [4]. It has also been observed that the size 2 has a greater tendency to kink [9]. There was no difference in the fibreoptic findings, the incidence of minimum $S\mathrm{po}_2$ or the incidence of clinical airway obstruction between patients up to 6.5 or between 6.6 and 10 kg. It is therefore suggested that the size 1 LMA can be used as an effective device in infants under 10 kg.

Table 2. Details related to laryngoscopic findings.

Laryngoscopic finding	Body weight (kg)		Insertion technique		Minimum $S\mathrm{po}_2$ (%)			
	−6.5	6.6–10	Standard	Reverse	100–95	94–90	89–85	Total
I	10	12	8	14	18	1	3	22
II	5	5	5	5	10	0	0	10
III	6	8	6	8	11	3	0	14
IV	3	1	1	3	2	1	1	4
Total	24	26	20	30	41	5	4	50

We have found by endoscopy that the LMA is positioned optimally in a comparatively small proportion (44%) of infants, compared with previous authors who have employed fibreoptic laryngoscopy in children of all ages (67% [1] and 49% [4]). This may be caused by a feature of the larynx in infants; the epiglottis is relatively narrow, short, and angled away from the axis of the trachea [6]. Nonetheless, as in other studies, the great majority of patients had a clinically patent airway following initial insertion. Ideally the epiglottis should not be visible at all in the LMA grille, but in this study we accepted fibreoptic grade II–IV, as long as the airway was clinically patent. There was no correlation between clinical airway patency and fibreoptic grade.

An unusual complication, herniation of the epiglottis through the grille of the LMA has been reported in an adult; this could result in epiglottic oedema and airway obstruction after extubation [10]. This study suggested that impinging of the epiglottis on the grille of the LMA (28%) is a relatively common phenomenon in infants, compared with that in children of all ages from our previous study (15%) [4], and this could result in epiglottic injury.

An important finding in infants was the high incidence of delayed airway obstruction, which was particularly associated with moving the patient. This tendency for the LMA position to deteriorate has not previously been reported, and may be related to the specific features of the infant larynx. Laryngoscopic findings and minimum $S\text{po}_2$ at the LMA insertion were not useful information to predict delayed airway obstruction, and we found that clinical assessment was the most useful guide to airway patency.

Insertion of the LMA in infants under 10 kg is a safe and straightforward procedure, which can be relied upon to produce a satisfactory clinical airway in the majority of cases. There is a tendency for the LMA position to deteriorate, and we would urge continuous vigilance for this complication if the LMA is to be employed in this group of patients.

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CASE REPORT

Profound hypotension following intravenous codeine phosphate

Three case reports and some recommendations

T. J. PARKE, P. R. NANDI, K. J. BIRD AND D. A. JEWKES

Summary

Three adults are described who developed life-threatening hypotension following intravenous codeine phosphate. It is recommended that codeine phosphate should not be given intravenously to adults.

Key words

Analgesics; codeine phosphate.
Complications; hypotension.

Codeine phosphate has retained a place in the treatment of moderate pain, despite the availability of new, highly potent synthetic opioids with minimal unpredictable adverse effects. In addition it is a popular analgesic for neurosurgical patients because of its relative lack of sedation and interference with pupillary size. The parenteral preparation of codeine phosphate currently available bears a label listing the intravenous route of administration as an alternative to intramuscular injection. Adverse reactions to intravenous codeine phosphate have been described in children, in whom its use is not recommended [1]. We describe three adults who developed severe hypotension following intravenous codeine phosphate.

Case histories

Case 1

A 17-year-old male, weighing 51 kg, was scheduled for six dental extractions, as a day case. He had previously been investigated for short stature but no cause had been found. He had received two uneventful anaesthetics for squint correction and tonsillectomy some years before.

He was prescribed no premedication. Anaesthesia was induced with alfentanil, thiopentone and suxamethonium, and following tracheal intubation was allowed to breathe spontaneously an oxygen/nitrous oxide/enflurane mixture. The patient remained stable throughout surgery, and at the end of the procedure his systolic blood pressure was 120 mmHg, which was identical to the pre-induction value. Codeine phosphate injection 50 mg (McCarthy 60 $mg.ml^{-1}$) was then given, undiluted, intravenously as a bolus. Almost immediately the patient became pulseless and grey, but the electrocardiograph (ECG) continued to show sinus rhythm at a rate of 90 $beat.min^{-1}$. The patient's lungs were ventilated with 100% oxygen and external cardiac massage started. Adrenaline (1 mg) was given intravenously. After 60 s the pulse became palpable and systolic blood pressure was measured at 40 mmHg. The patient remained in sinus rhythm at a rate of 90 $beat.min^{-1}$. Ephedrine 15 mg and atropine 0.6 mg were administered intravenously and 4 min later the systolic blood pressure was 70 mmHg, but a further 5 min elapsed before the systolic blood pressure reached 100 mmHg (Fig. 1). At no time did any bronchospasm or rash develop, and there was no increase in body temperature. The patient's trachea was extubated and he was admitted for observation overnight. He remained stable and his ECG was normal. He was discharged the next day, fully recovered, with written instructions that he was allergic to codeine phosphate injection.

Case 2

A previously fit, 16-year-old female was scheduled for myringoplasty. She was premedicated with lorazepam. Anaesthesia was induced with thiopentone and vecuronium and maintained with enflurane in nitrous oxide and oxygen

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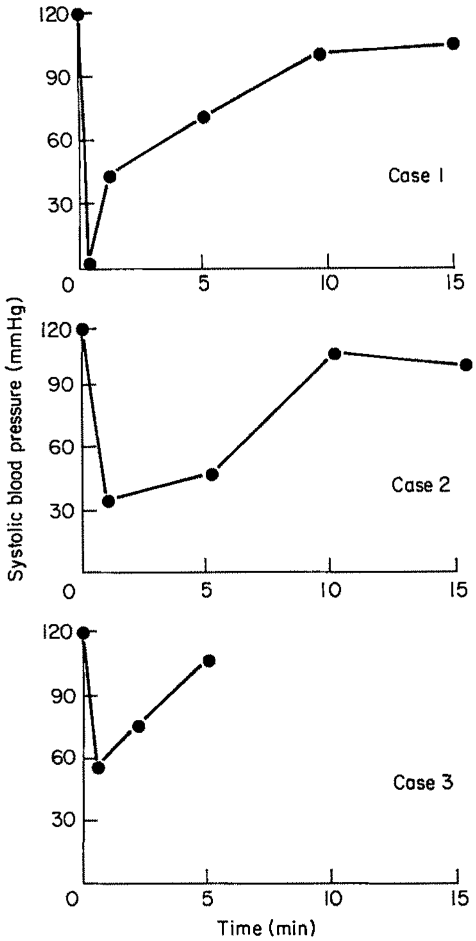

Fig. 1. Plot of systolic blood pressure against time. Intravenous codeine was given at time 0 minutes in all three cases.

following tracheal intubation. Ten min after surgery was started the consultant anaesthetist drew up 60 mg of codeine phosphate (McCarthy 60 mg.ml^{-1}) which he intended to give intramuscularly. He then read on the ampoule that the injection was also suitable for intravenous administration, and gave 60 mg undiluted as a bolus. Before the injection her systolic blood pressure was 120 mmHg. Almost immediately the patient developed generalised erythema and a weak thready pulse (130 beat.min^{-1}). Her systolic blood pressure fell to around 35 mmHg and the ECG continued to show sinus rhythm, but no bronchospasm developed. She was given intravenous adrenaline (0.5 mg), oxygen and colloid solutions, followed by intravenous chlorpheniramine and hydrocortisone, but did not require cardiac massage. Five min after the codeine injection her systolic blood pressure was 50 mmHg, and after 10 min it had increased to 110 mmHg (Fig. 1). Her trachea was extubated after 30 min and she was discharged home fully recovered the next day, with written advice that she was allergic to codeine phosphate. The myringoplasty was abandoned and performed 3 months later. The same consultant anaesthetist administered the anaesthetic. The lorazepam premedication was changed to pethidine and atropine, and no opioids were given intra-operatively. Thiopentone, vecuronium, and enflurane were given as before and anaesthesia proceeded uneventfully.

Case 3

A 45-year-old woman, ASA grade 1, presented for excision of a right acoustic neuroma. A previous general anaesthetic had been unremarkable. No premedication was ordered. Anaesthesia was induced with thiopentone followed by suxamethonium, and the trachea was intubated after spraying the laryngeal inlet with 4 ml lignocaine 4%. The lungs were ventilated with 50% nitrous oxide in oxygen and supplemental isoflurane. Neuromuscular blockade was maintained with tubocurarine. Blood pressure was monitored continuously via a radial arterial line. The patient was placed in the left lateral position. Systolic blood pressure was maintained at 80–90 mmHg with incremental doses of labetalol.

During surgical closure the blood pressure was restored to 120/80, neuromuscular block reversed with neostigmine and glycopyrronium and spontaneous breathing re-established. It is customary in our unit to give codeine phosphate 0.5–1.0 mg.kg^{-1} by intramuscular injection at the stage of closure of the galea, but on this occasion the injection was overlooked until late in the course of the operation. It was therefore decided to administer a slow bolus injection of codeine phosphate intravenously. However, following the administration of approximately 10 mg of codeine phosphate the arterial blood pressure decreased from 100/55 to 55/35 mmHg over the course of 30 s. There was an associated decrease in heart rate from 60 to 50 beat.min^{-1}. The injection was stopped immediately; the lungs were ventilated with 100% oxygen and the infusion of crystalloid (compound sodium lactate solution) increased, 300 ml being given over 1 min. The blood pressure increased rapidly to 74/45 mmHg, and recovered to normal over the next 5 min (Fig. 1). The hypotensive episode was not associated with hypoxaemia or a rash. The patient's recovery and postoperative course were unremarkable. She received several intramuscular injections of codeine phosphate in the postoperative period without experiencing any adverse reaction.

Discussion

In 1983, Shanahan reported three cases of severe adverse reactions to intravenous codeine phosphate in children (age 1 year, 20 months and 7 years) [1]. This was attributed to histamine release and was thought to be dose related. As in case 3, all the children had received the drug intramuscularly either before or after the intravenous dose, without adverse effects. The authors stated that, in their experience, adults had shown no adverse effects following intravenous codeine 0.25–0.75 mg.kg^{-1}. They thus recommended that intravenous codeine phosphate should be avoided in children, although they gave no upper age or weight limit. In 1984 McCarthy altered the drug licence, replacing 'iv/im' with 'im' on all but the 60 mg.ml^{-1} ampoules, in the belief that the latter would not be used in children.

Such adverse reactions in adults do not seem to have been reported before. The adverse reaction service provided by the Committee on the Safety of Medicines to which these cases were reported does not have a category for codeine phosphate injection. Likewise the supraregional NHS protein reference laboratory based at Sheffield has no other report of a similar incident. However, there seems little doubt that in the three cases described, serious hypotension occurred which was related to the bolus administration of intravenous codeine.

A search of the literature has revealed only four reports of the use of intravenous codeine in adults. In 1948 Meals gave 30 mg of codeine sulphate every 30 min to 93 adults, undergoing thiopentone anaesthesia, uneventfully [2]. However, this was given slowly over 2 min. Furthermore, the salt used may be important [3], and codeine sulphate is no longer available. In 1953 Brown used codeine phosphate in 15 mg doses intravenously in 100 adults without ill effect [4]. However, in one patient a 30 mg bolus resulted in a 'marked fall in blood pressure which lasted about 40 min.' More recently, codeine phosphate has been given intravenously to adults in pharmacokinetic studies, but only by slow infusion [5, 6].

Rapid injection may be responsible for the reactions we describe and, as in Shanahan's cases, histamine release seems to be the most likely explanation. The absence of a rash or bronchospasm does not exclude histamine release, and hypotension may occur as the sole manifestation [7]. Drugs may release histamine by a direct action on the mast cell, by an IgE-mediated, immunological mechanism, (implying previous sensitisation), or by nonimmune complement activation. The clinical severity of the reaction is unrelated to the mechanism by which histamine is released, but is correlated in part to the amount of histamine released [7]. Direct release of histamine from the mast cell occurs with opioids, the amount released being related to the dose and speed of injection. Codeine in equi-analgesic doses is a more potent histamine releaser than morphine, and in consequence the American Medical Association's Drug Evaluations state that codeine should not be administered intravenously [8]. This, however, is the only reference work to offer such categorical advice. Hypotension caused by opiate alkaloids is mainly as a result of vasodilatation and peripheral pooling of blood and appears after a latency of 15–20 s which is typical of histamine releasers [9]. The hypotension is increased by hypovolaemia, phenothiazines, head-up posture, and general anaesthesia [10]. These last two factors were present in the cases described, and Shanahan commented that the more serious reactions occurred in the two children receiving general anaesthesia, and postulated that halothane enhanced the depressant effects of codeine [1]. Animal studies have suggested that the prolonged hypotension induced by intravenous opioids cannot be fully explained by the plasma histamine levels [9]. Delayed cardiovascular recovery was a feature of two of the cases described. It is possible that opioids might directly depress the myocardium or vasomotor centre, in addition to histamine mediated effects.

Use of intravenous codeine is never clinically indicated, and bolus injection would appear to be associated with a significant risk of severe hypotension. In the light of the above cases, we believe that codeine should not be given intravenously to any patient, irrespective of their age. The labelling on the ampoule should be changed to reflect this.

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Anaesthesia, 1992, Volume 47, pages 855–856

CASE REPORT

Laryngospasm during transtracheal high frequency jet ventilation

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Summary

A 74-year-old woman developed severe cardiovascular depression during percutaneous transtracheal high frequency jet ventilation for laser surgery of the epiglottis. This was found to be caused by acute airway obstruction secondary to severe laryngospasm. We recommend profound neuromuscular blockade during percutaneous transtracheal jet ventilation, in order to prevent this complication.

Key words

Anaesthetic techniques; intravenous.
Ventilation; high frequency, jet, percutaneous transtracheal ventilation.
Complications; laryngospasm, barotrauma, cardiovascular depression.

Patients undergoing percutaneous transtracheal high frequency jet ventilation (HFJV) have an increased risk of barotrauma and circulatory depression when upper airway obstruction occurs. Tumours of the trachea or larynx, surgical debris or blood may predispose to this, but more commonly obstruction is caused by anatomical factors; in the anaesthetised or sedated patient the tongue [1], the soft palate or the epiglottis [2] may approximate to the posterior pharyngeal wall. We report an unusual case in which severe laryngospasm, occurring during laser surgery for an epiglottic tumour, resulted in airway obstruction during expiration and acute circulatory failure.

Case history

A 60 kg, 74-year-old woman was scheduled for laser surgery to a tumour of the epiglottis. Symptoms consisted of 'thick' speech and occasional dyspnoea, especially in the morning. She was otherwise well and had no history of cardiac or pulmonary problems. Routine biochemical and haematological investigations showed no abnormality.

Pre-operative sedation was achieved with clorazepate 25 mg orally given 60 min before the induction of anaesthesia. Monitoring consisted of electrocardiograph (ECG), pulse oximetry, capnography and radial arterial pressure recording. Neuromuscular blockade was assessed with a nerve stimulator using the train-of-four (TOF) technique. After pre-oxygenation, anaesthesia was induced with propofol 80 mg and fentanyl 75 μg intravenously. After it was ascertained that inflation of the lungs was possible via a mask, atracurium 25 mg was administered and anaesthesia was maintained with a propofol infusion at a rate of 500 $mg.h^{-1}$ with fentanyl given as necessary. Four minutes later, a 13-G intratracheal catheter (VBM, Medizintechnik GmbH, Sulz am Neckar, West Germany) [3] was inserted percutaneously through the cricothyroid membrane under direct vision, using a fibreoptic bronchoscope that had been introduced orally and was positioned just below the vocal cords. Percutaneous transtracheal HFJV was initiated using a jet ventilator (Model VS 600, Instrumental Development Corporation, Switzerland) with a driving pressure of 274 kPa at a frequency of 150 per min and an inspiratory:expiratory ratio of 1:2. Oxygen 100% was delivered and a size 4 oropharyngeal airway was inserted to assist expiration.

When laser surgery was started 10 min later, the epiglottis appeared to be grotesquely swollen and the surgeon was unable to visualize the laryngeal inlet through the laryngoscope. Laser surgery proceeded without difficulty for 20 min, at which stage the pulse oximeter suddenly failed to register and the systolic blood pressure decreased rapidly to 20–30 mmHg with a heart rate of 30 $beat.min^{-1}$. Simultaneously, the movement of the chest wall produced by the HFJV stopped. Ephedrine, given in three separate doses of 10 mg, did not improve the blood pressure. Just before this catastrophic event, atracurium 5 mg had been administered because TOF monitoring showed that three out of four twitches were present. On the assumption that airway obstruction had occurred, the anaesthetist urged the surgeon to re-establish its patency. The surgeon thought

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that there was no anatomical reason for complete airway obstruction, but while attempting tracheal intubation, managed to visualize the posterior part of the vocal cords, which were noted to be firmly closed. Suxamethonium 100 mg was injected and 30 s later a sound was heard of a large quantity of gas escaping from the airway, the blood pressure rapidly returned to normal and the pulse oximeter again registered 100% oxygen saturation. Surgery was completed without further complication and post-operatively the patient showed no evidence of barotrauma.

Discussion

Percutaneous transtracheal high frequency jet ventilation is an accepted method for artificial ventilation of the lungs during certain ENT procedures, particularly laser surgery of the larynx. Alternative techniques, using a tracheal tube, carry the risk of setting fire to the tube and subsequent damage to the patient's airway. In addition, optimal surgical conditions often cannot be guaranteed. In our institution, the method of percutaneous transtracheal HFJV through a 13-G catheter is well established and, with the additional precaution of placing the cannula under direct vision using a fibreoptic bronchoscope, no complications such as bleeding, submucosal air insufflation or posterior tracheal wall lesions have occurred. It is possible to maintain satisfactory ventilation by means of transtracheal HFJV even when small-gauge catheters are used because of the high driving pressure [4, 5]. However, passive exhalation requires more time and is dependent on patency of the airway. Occlusion of the expiratory pathway rapidly leads to hypoventilation, manifested by hypercarbia and hypoxaemia, and may interfere with cardiac output by increasing the intrathoracic pressure, with the risk of producing serious barotrauma to the lungs. Upper airway obstruction is usually associated with anatomical, functional or pathological supraglottic lesions [3] such as epiglottitis, tumours, oedema and trauma. During ENT surgery, obstruction secondary to blood and tumour debris has also been reported [6]. In our experience, in patients with a normal anatomy, the tongue is usually the cause of obstruction, because of displacement towards the posterior pharyngeal wall. Because of this we always place a nasal or oral airway (Guedel or Wendel tube) until the surgeon is ready to introduce the operating laryngoscope.

The airway occlusion seen in this patient was caused by laryngospasm rather than by the grossly swollen epiglottis. Insufficient depth of anaesthesia, visceral pain and mechanical stimulation by blood or secretions may have led to the development of a gas-tight closure of the larynx. The diagnosis was difficult, because laryngospasm is very uncommon under these circumstances, since the glottis is usually visible and may even be spread by the operating laryngoscope. In addition, neuromuscular blockade was thought to be adequate.

It is interesting that laryngospasm under these conditions can so rapidly lead to cardiovascular failure. The laryngospasm which occurs in a spontaneously breathing patient or during mask ventilation may be relieved by positive pressure ventilation, head lift and jaw tilt. In contrast, during transtracheal HFJV, increasing the subglottic pressure is of no benefit and carries the risk of rapid cardiovascular impairment and barotrauma to the lungs.

During transtracheal jet ventilation it is essential that the expiratory pathway is unobstructed. In addition, adequate neuromuscular blockade should be provided to avoid the danger of laryngospasm. If attention is paid to these details, the risks of this technique is minimised.

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Anaesthesia, 1992, Volume 47, pages 857–858

CASE REPORT

Reversible paraplegia following coeliac plexus block

S. S. JABBAL AND J. HUNTON

Summary

Permanent paraplegia following coeliac plexus block has been reported on several occasions. We report a case of reversible paraplegia following coeliac plexus block.

Key words

Anaesthetic techniques, regional; coeliac plexus block.
Complications; paraplegia.

Case history

A 53-year-old man presented with a 6 month history of loss of weight, anorexia, nausea, vomiting and severe abdominal pain. A computerised axial tomograph (CAT) scan of his abdomen showed a number of masses in the region of the head of the pancreas, and a diagnostic laparotomy revealed an 8 cm × 8 cm hard mass in the posterior aspect of the right lobe of the liver adjacent to the inferior vena cava. In addition, there were two small nodules in the left lobe of liver, a small 'chain of pearls' of tumour at the porta hepatis and a 3 cm × 4 cm tumour anterior to the right kidney but separated from the head of the pancreas. The pancreas appeared clear of tumour on palpation. The omentum had four large nodules which were excised. Histology showed the excised nodes to be a poorly differentiated adenocarcinoma of uncertain origin. As this tumour was unlikely to be responsive to chemotherapy or radiotherapy, a coeliac plexus block was offered to the patient to relieve the severe upper abdominal pain, which was worse in the right loin and radiated into the chest.

A neurolytic coeliac plexus block was carried out under X ray control in the prone position using 2 × 20 ml of alcohol 50% in bupivacaine 0.25%. A radiological dye was not used. Propofol 200 mg was given intravenously and oxygen and nitrous oxide was administered by face mask. Electrocardiogram, oxygen saturation, and blood pressure were monitored.

Following the procedure the patient was free of the upper abdominal pain although a little sleepy from the anaesthetic. However, he was complaining of pain at the injection site and was given papaveretum 15 mg intramuscularly. Approximately 1 h later he complained that his right leg felt peculiar and he had paraesthesia. This became worse over a short period and spread to the left leg. Paraesthesia intensified overnight and by the following morning he had, on the right side, complete loss of flexion and extension of the hip, gross weakness of flexion and extension of the knee, gross weakness of foot dorsiflexion and weak plantar flexion. The left leg, although a little weak, was much better than the right leg. He continued to complain of paraesthesia, mainly in the right leg, and of numbness of the buttocks. On examination, sensation to light touch was normal, although with dysaesthesia. Reflexes were brisker on the right than the left and both plantar responses were flexor. Neurosurgical opinion suggested a L_{1-3} paraparesis. Myelography did not reveal any spinal cord compression and the cause of this complication was attributed to a vascular incident.

Physiotherapy was started immediately and a slow improvement occurred with the patient able to walk with a stick within a week of the event and discharged from hospital 10 days after the coeliac plexus block with minimal neurological deficit. The block initially produced good pain relief, but this only lasted a few weeks, after which he required oral analgesics in high dosage. He died, at home, 1.5 years later as a result of his malignancy.

Discussion

In 1914 Kappis first described percutaneous coeliac plexus block. Since then variations and refinements of his tech-

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nique have been proposed including the use of X ray screening and CAT scanning.

The vascular supply of the spinal cord was first studied in 1882 by Adamkiewicz. He described the arteria redicularis magna (the artery of Adamkiewicz), the largest of the medullary feeding vessels for the supply of the lumbar spinal cord. It occurs on the left side, in about 80% of cases at between vertebral levels T_7 and L_4, although it is usually found at the T_9 to T_{11} level. The artery of Adamkiewicz is considered important but its ligation in Rhesus monkeys was not followed by any subsequent neurological consequences [1]. The circulation after ligation is maintained by other anterior medullary arteries, their number varying from two to 17, but there are rarely more than nine [2].

Pheumothorax [3], chylothorax [4], damage to the kidney [5] and pleural effusion after CAT scan-guided coeliac plexus block [6] have been reported. Brown and Moore [5] described seven cases of paraplegia, but we found a total of seven reports of neurological complications following coeliac plexus block, of which four were about paraplegia [7–13].

Galiza and Lahiri [8] reported a case that involved the use of phenol, which led to complete paraplegia with a sensory level at T_{12}. The aetiology was postulated to be secondary to an ischaemic injury to the spinal cord. The patient developed intestinal obstruction and died following a haematemesis. Thompson [9] reported on a series of 100 coeliac plexus blocks in which one patient developed partial leg paralysis. This procedure was performed in the lateral position without the use of X ray screening. The probable cause of this lesion was believed to be direct irritation of the lumbar nerve roots by alcohol. Cherry and Lamberty [11] reported a case of paraplegia with a sensory level at T_{11-12}. The sensory loss was variable, whereas the motor deficit was profound. X ray screening was used in this case and once again the postulated cause of the neurological lesion was ischaemia of the cord secondary to damage or spasm of the artery of Adamkiewicz. Ten days after the procedure the patient developed acute upper abdominal pain and died soon afterwards. Woodham and Hanna [12] reported a block performed under X ray screening with the patient prone. Alcohol was used on the left side and bupivacaine on the right. Following the block there was total flaccid paralysis except for a flicker of movement in the left second toe. There was minimal change in the patient's neurological condition in the 2 weeks after the procedure and the patient died 2 months later. A myelogram performed on the day after the procedure was normal and again the presumptive diagnosis was made of ischaemia of the cord secondary to damage to the artery of Adamkiewicz.

Van Dongen and Crul [13] described a patient in which a coeliac plexus block with alcohol 48%, performed under X ray control, resulted in paraplegia. Ischaemia of the spinal cord, due to damage to the arterial blood supply, was thought to be the cause. Bowen Wright [14] has suggested that care should be taken to avoid injection into the spinal artery during coeliac plexus block and Churcher [15] has expressed concern about the possibility of more reports of paraplegia occurring before a rational approach to the problem is adopted. In our case, radio-opaque dye was not used to confirm the position of the needles, as lateral and antero-posterior X ray screening and negative blood or cerebrospinal fluid aspiration was thought to provide adequate information. We considered the possibility of direct injection of alcohol into cerebrospinal fluid or an artery to be very unlikely. Mechanical damage to the artery by the needles is a possibility, but the exact cause of the paraplegia and the recovery remained uncertain.

Although we do not dispute the claims that the most probable cause of paraplegia in all the cases cited was ischaemia of the spinal cord secondary to damage or spasm of the artery of Adamkiewicz, we strongly suggest that an autopsy should be carried out if a patient dies with paraplegia shortly after a coeliac plexus block has been performed. We also strongly support Churcher [15] and agree with his concern about probabilities of more reports of paraplegia and suggest that the possibility of this complication should be kept in mind before offering neurolytic coeliac plexus block to a patient. We suggest that every patient should be informed of the possibility of this rare but serious complication.

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Anaesthesia, 1992, Volume 47, pages 859–861

CASE REPORT

Repeated unilateral epidural blockade

A. F. McCRAE, A. WHITFIELD AND J. H. McCLURE

Summary

Unilateral epidural analgesia occurring in a parturient three times in successive pregnancies is reported. Possible causes are reviewed, and clinical and radiological evidence in support of the most likely explanation are presented.

Key words

Anaesthetic techniques, regional; epidural.
Complications; unilateral.

It is now widely accepted that a dorsomedian connective tissue band exists within the epidural space. It has been demonstrated by computerised axial tomo CT-epidurography [1, 2], using polyester resin injected into the epidural space of cadavers to form casts [3, 4], and the endoscopic technique of epiduroscopy developed by Blomberg [5]. The clinical history and X ray findings in the following case support the existence of such a structure.

Case history

A 22-year-old, 150 cm woman, para 3, weighing 71 kg requested epidural analgesia for labour. Epidural analgesia was used in each of her three previous labours, but at the time the old case notes were unavailable. The patient indicated that the epidural in her first labour was totally successful, but that during the second and third labours the epidural catheter required resiting due to unilateral blockade. However, this led to apparent adequate analgesia. The fourth pregnancy had been uneventful, and the patient's past medical history was otherwise unremarkable. There was no history of any chronic back problem or damage to the spine.

With the patient in the sitting position, a midline approach to the epidural space was made at the first lumbar interspace using a 16 g Tuohy needle. The epidural space was located at 4 cm by loss of resistance to injection of N-saline. An end-hole catheter was introduced 3 cm into the epidural space in a cephalad direction without difficulty. A test dose of 4 ml of 0.5% bupivacaine was given through the catheter with no evidence of intravascular or subarachnoid injection, and 5 min later a further dose of 6 ml 0.5% bupivacaine was given. Fifteen minutes later a sensory block had developed from T_4–L_3 on the left side only. At 30 min there was still no evidence of sensory block on the right side and motor block had not developed on either side. The patient was therefore turned onto her right side, the catheter was withdrawn 1 cm and a top-up of 6 ml 2% lignocaine was given. Fifteen minutes after this top-up the block remained confined to the left side and extended from T_1–L_3, associated with Bromage grade 1 motor block. At this stage the patient complained of tingling in her left hand, feeling her wedding ring tight and of being unable to get enough breath to blow her nose. There was no sign of a Horner's syndrome on the left. Arterial blood pressure was well maintained throughout, the lowest systolic reading being 103 mmHg.

The patient declined to have the epidural resited, and in view of the very high block on the left side, it was felt inappropriate to use any more local anaesthetic. Analgesia was, therefore, provided with incremental intravenous pethidine.

Thirty minutes after the last top-up with lignocaine and after pethidine had been given, the patient indicated that she now felt some numbness on her right side. On testing she was found to have a just discernable sensory block from T_5–L_2 on the right and a dense block from T_1–L_3 on the left. At 45 min the sensory block extended from C_7–L_4 on the left and C_8–L_4 on the right, although the block on the right was less dense and patchy with a missed segment at L_1. Further analgesia was requested 75 min following the last top-up. At this stage the right-sided block had disappeared but a sensory-only block remained on the left from T_1–L_2. Since the previous top-up had eventually given

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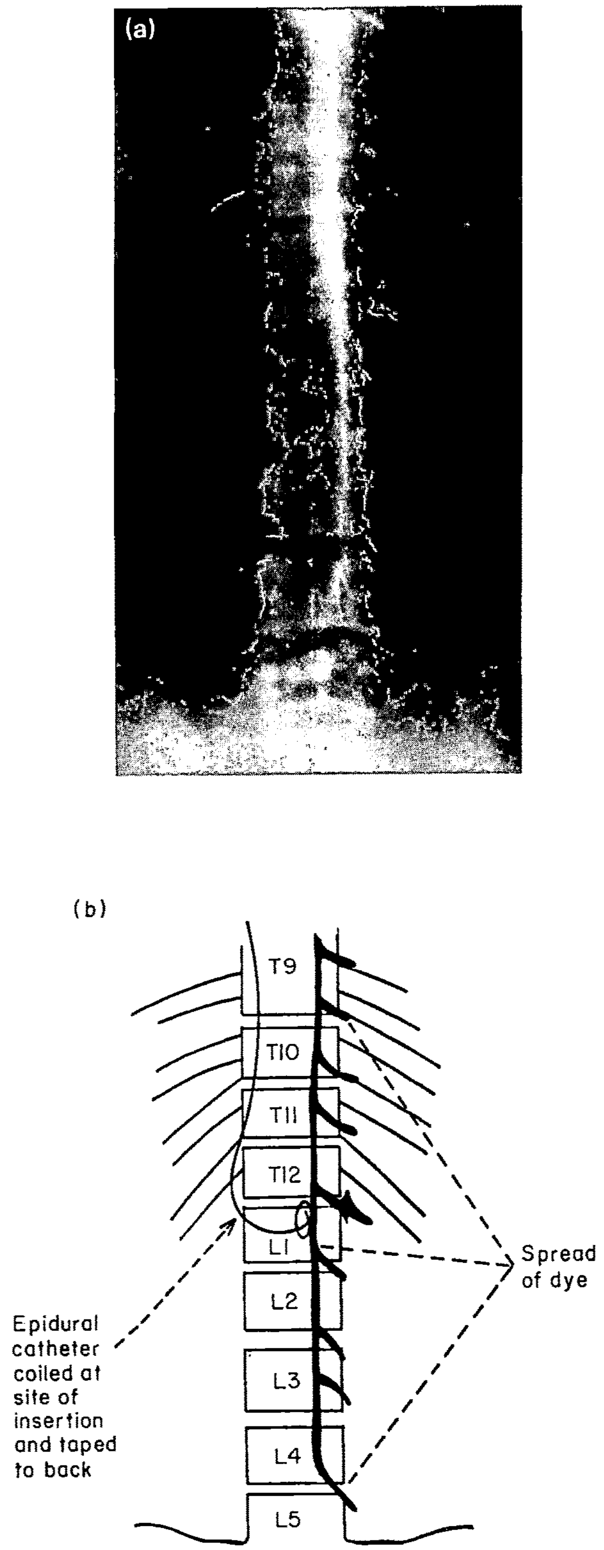
(a)
(b)
T9
T10
T11
T12
L1
L2
L3
L4
L5
Spread of dye
Epidural catheter coiled at site of insertion and taped to back

Fig. 1. (a) and (b). Contrast medium spreading from the fourth lumbar to the ninth thoracic vertebra on the left side only, with contrast entering most of the nerve sheaths at these levels.

bilateral analgesia, a further 4 ml of 2% lignocaine was given and this was repeated after 15 min. This produced a block from C_8–L_4 on the left side but no block on the right.

At delivery, the baby had Apgar scores of 5 and 9, at 1 and 5 min and received naloxone. One hour later the mother had full return of sensation and motor power.

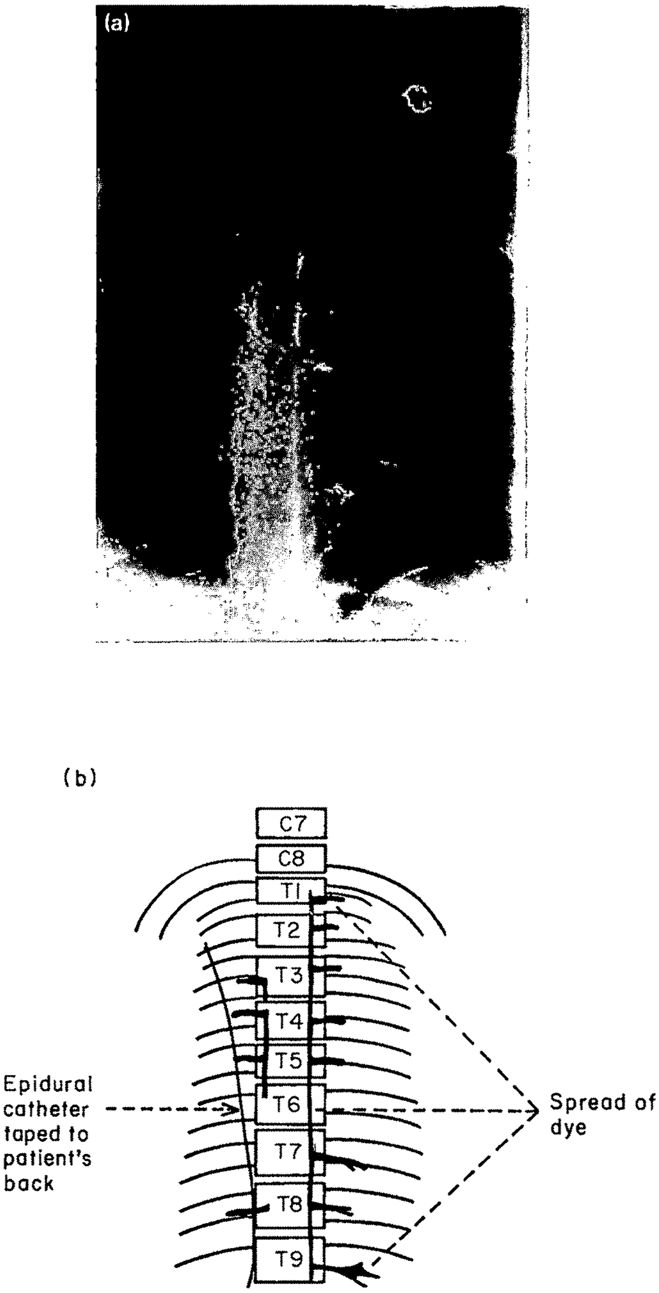

Fig. 2. (a) and (b). Contrast medium spreading from the ninth thoracic to the first thoracic vertebra on the left side, crossing to the right at the level of the third thoracic vertebra and seen in decreasing amounts down to the eighth thoracic vertebra.

The epidural catheter was left *in situ* until the following morning when an epidurogram was performed using 9 ml of nonionic contrast medium ('Niopam'). Anteroposterior views of the thoraco-lumbar spine were obtained. These showed spread of contrast medium on the left side with spillage into the sheaths of the nerve roots as far up as T_1. There was also a small amount of contrast on the right side from T_2–T_4. These appearances are suggestive of a midline septum dividing the epidural space.

Discussion

The reported incidence of unilateral epidural block in obstetric patients varies from 5–21% [6, 7], with persistent unilateral block in 1–2% of cases [7–9]. Using end-hole catheters we estimate an incidence of 3–5% of all epidurals in our unit.

Possible causes of unilateral block include anatomical defects, variations in technique, catheter type and most commonly the position of the epidural catheter. Congenital abnormality of the spine [3] or the presence of epidural adhesions [10–12] may limit spread. Slow injection of the local anaesthetic solution in the lateral position [13], or deviation of the Tuohy needle from the midline (often associated with an increased distance from skin to the epidural space [14]) is more likely to produce an unequal block. Passage of the epidural catheter to the paravertebral region [15], the anterior epidural space [13], or to the subdural space may also produce a unilateral block. The incidence of subdural cannulation has been estimated as 0.82% [16], typically producing a delayed block with extensive spread [17].

In this case, the depth of the epidural space was 4 cm and only 3 cm of catheter was left in the space. Lateral placement and excessive catheter length are, therefore, unlikely causes of unilateral block. An end-hole catheter was used, although it is uncertain whether or not this is associated with a higher incidence of unilateral block [18, 19]. A block from T_1–L_4 with 4+6 ml bupivacaine is more consistent with epidural administration than subdural.

In our case, the epidurogram shows contrast spreading on the left side from T_1–L_4 and confined to the left side, except at T_3, where there is spillage to the right side with decreasing amounts of contrast visible on the right down to T_8. Contrast can be seen entering most of the nerve sheaths between T_1 and L_4 on the left producing the typical 'tree' appearance of dye in the epidural space.

On retrieval of old notes it was discovered that both previous unilateral epidurals also produced only left-sided block. The history of satisfactory block following resiting on previous occasions raises the possibility of a dorsal midline septum in the epidural space as the cause of unilateral spread.

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Anaesthesia, 1992, Volume 47, pages 862–863

CASE REPORT

Profound desaturation following vomiting on induction

A case for routine pre-oxygenation

A. G. HEAD-RAPSON, S. J. RALSTON AND S. L. SNOWDON

Summary

Whilst participating in a clinical trial, a patient vomited during induction of anaesthesia. Subsequent analysis of the continuous record of oxygen saturation showed precipitous desaturation.

Key words

Anaesthesia; induction.
Complications; regurgitation, hypoxia.
Equipment; pulse oximeter.

Recently, there have been a number of articles published showing that desaturation is a common phenomenon during inhalational induction of anaesthesia and that it may be abolished by pre-oxygenation [1–4]. This desaturation is thought to be of little significance in an uncomplicated induction, but it is always stated that should things go awry, one is already on the 'knee' of the haemoglobin–oxygen dissociation curve, and desaturation will then be immediate and profound. We report a case in which we were able to capture such an incident.

Case history

A 54-year-old, ASA 1 male weighing 84 kg presented for an elective cystoscopy. There was no history of reflux, and he had been starved since midnight. He had given informed consent to participate in a clinical trial [4], and was randomised to receive propofol for the induction of anaesthesia. During the induction a continuous record of oxygen saturation was made with an Ohmeda 5250 RGM, and chart recorder.

Following the administration of propofol 2.5 mg.kg,$^{-1}$ he was apnoeic for a short period, which was characteristically associated with a moderate desaturation, and then started to breathe, after which there was an improvement in $S\text{po}_2$. There was no evidence of airway obstruction, when without warning he vomited a large quantity of clear fluid. His trachea was intubated promptly once suxamethonium 100 mg had been given, and intermittent positive pressure ventilation (IPPV) instituted, initially with 100% oxygen. Tracheal aspiration produced only minimal secretions. Anaesthesia was continued with nitrous oxide, oxygen and isoflurane, the cystoscopy was performed and his trachea was extubated while he was in the lateral position following further tracheal suction. His postoperative course was uneventful and he was discharged the following day.

Once the incident was over we were able to examine the tracing of the events at induction (Fig. 1). This clearly shows the profound hypoxaemia that rapidly develops if an incident occurs when an $S\text{po}_2$ is already reduced by the physiology of mask induction.

Discussion

Pre-oxygenation is routinely performed in many countries, but in this country it is only with the fairly recent widespread availability of the pulse oximeter that the changes in $S\text{po}_2$ associated with the inhalational induction of anaesthesia in patients who have not been pre-oxygenated have become apparent.

Laycock *et al.* [1] were 'surprised and alarmed at the degree of hypoxaemia' they found in their audit of children undergoing general anaesthesia for routine elective surgery. They placed no restriction on the type of premedication or induction technique for the children, and in the 108 inductions they surveyed, 29 patients developed an $S\text{po}_2$ of less than 90%, seven patients an $S\text{po}_2$ of less than 80%, and the lowest recorded $S\text{po}_2$ was 32%. None of these patients was pre-oxygenated.

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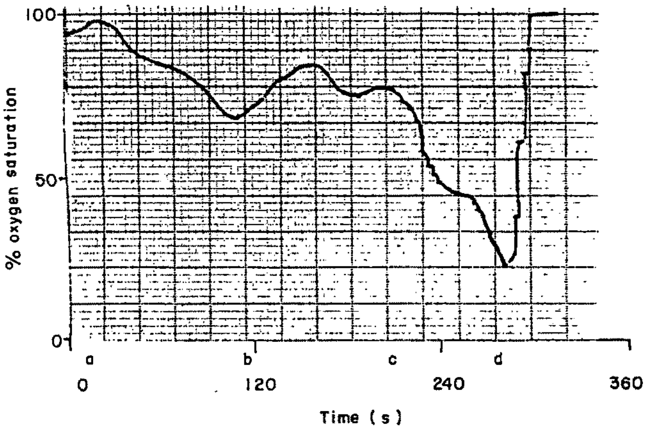

Fig. 1. Chart recording of oxygen saturation during induction in a patient who vomited. Induction was at 0 s. There is a brief initial increase in oxygen saturation, explainable by the increased FiO_2 as the facemask is applied. Characteristic desaturation is seen following a period of apnoea. This improved with manual ventilation at 120 s. Vomiting occurred at point (c), after which a dramatic decrease in saturation is seen. Note the rapid improvement following tracheal intubation and ventilation with 100% oxygen (at point (d)).(a) initial increase in saturation; (b) desaturation improving with ventilation; (c) patient vomits; (d) intubated.

Thorpe *et al.* [2] studied three groups of patients presenting for inhalational anaesthesia, in a more controlled manner. Group A received no added oxygen but were allowed to breathe 66% nitrous oxide in oxygen after the initial period of apnoea, group B were pre-oxygenated with a few normal breaths of 100% oxygen prior to induction, and group C were oxygenated after the loss of the eyelash reflex. Six patients in group A and three in group C became hypoxaemic (which they defined as an Spo_2 of $< 90\%$). None of the patients in the pre-oxygenated group became hypoxaemic.

Moller *et al.* [5] investigated 296 inpatients in a study that monitored Spo_2 during the entire anaesthetic. More than half (53%) of their patients developed what they called 'mild hypoxaemia' (Spo_2 86–90%), 20% had episodes of hypoxaemia with an $Spo_2 < 81\%$ at some point during the anaesthetic. They concluded that 'during routine anaesthesia, hypoxaemia is more common and severe than previously assumed', and advocated routine pre-oxygenation for all patients.

Perhaps the most convincing evidence to date that desaturation is common during inhalational induction, and that it is abolished by pre-oxygenation, comes from the recent study by Kung *et al.* [6] in which they compared two groups of healthy patients, one of which was pre-oxygenated. None of the patients in this group desaturated, while 40% of those in the non-preoxygenated group did; some to as low as 50%.

Other studies have confirmed both that desaturation is a far from rare event during inhalational induction anaesthesia, and that its occurrence can be abolished with even a few breaths of pre-oxygenation [3, 4].

That pre-oxygenation is not routinely performed in the face of this evidence is surprising. In a questionnaire sent recently to all anaesthetists in this hospital, of the 28 respondents 14 felt that pre-oxygenation was not routinely necessary, or desirable, on the grounds of patient discomfort. The remaining 14 anaesthetists felt that routine pre-oxygenation was desirable, but only seven of them actually do it and they were mainly of senior house officer grade.

A strong additional argument for routine pre-oxygenation is the avoidance of rapid hypoxaemia which is associated with events such as that described in this case report.

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Anaesthesia, 1992, Volume 47, pages 864–865

CASE REPORT

Anaphylactoid reaction to propofol

S. P. McHALE AND K. KONIECZKO

Summary

A case of an anaphylactoid reaction following the induction of anaesthesia is reported. Subsequent intradermal testing suggested propofol to be the causative agent.

Key words

Anaphylaxis; propofol.

Case history

A 46-year-old West Indian man with a pyloric stricture was admitted for polyagastrectomy. He had not had a general anaesthetic before, and his only medication was ranitidine 300 mg at night. Pre-operative examination and investigations were unremarkable, haemoglobin electrophoresis was normal and he was not noted to be an atopic individual. He was premedicated with papaveretum 20 mg and hyoscine 0.4 mg 1 h before induction of anaesthesia; this made him sleepy but rousable. In the anaesthetic room his arterial blood pressure was 120/85 mmHg and heart rate 80 beat.min^{-1}. Following pre-oxygenation and with the application of cricoid pressure, anaesthesia was induced by propofol (170 mg), to which lignocaine (20 mg) had been added. Suxamethonium (100 mg) was given to facilitate tracheal intubation which was easy. A propofol infusion was commenced at a rate of 10 mg.kg^{-1}.h^{-1}.

Initially there appeared to be decreased air entry to the left lung with an expiratory wheeze at the apex, and the tracheal tube was withdrawn slightly. The patient's lungs were manually ventilated with some difficulty and atracurium (35 mg) was administered. At this stage the patient's heart rate was 156 beat.min^{-1}, systolic arterial blood pressure 40 mmHg, peripheral oxygen saturation 84% (100% oxygen) and end-expiratory carbon dioxide tension 5.8%, with a marked upward slope on the carbon dioxide curve. A rash was noticed on the patient's abdomen and arms, which was difficult to discern because of his skin colour.

Immediate treatment consisted of infusion of Haemaccel (500 ml) and intravenous ephedrine (30 mg) which was immediately available. The propofol infusion was stopped. The patient's blood pressure improved rapidly to 100 mmHg systolic, heart rate gradually decreased to 65 beat.min^{-1}, peripheral oxygen saturation increased to 100% (50% oxygen), and end-expiratory carbon dioxide tension dcreased to 5.0% with a flat plateau on the tracing. Hydrocortisone (100 mg) was given intravenously and the operation commenced.

Anaesthesia was maintained with oxygen/nitrous oxide and isoflurane; further neuromuscular blockade was achieved with vecuronium and the operation was completed 90 min later. Recovery was uneventful and the patient went home after 9 days.

Investigations

A blood sample taken 24 h after the incident showed an IgE level of 5000 μ.ml^{-1} (normal up to 200 μ.ml^{-1}), C3 70 mg.dl^{-1} (normal 77–163 mg.dl^{-1}), C4 28 mg.ml^{-1} (normal 14–42 mg.ml^{-1}), and CH50 of 1/64 (normal $\geqslant$ 1/64). The high level of IgE may suggest an atopic individual but this was not the case with this patient.

Six weeks later the patient was tested intradermally against a variety of anaesthetic agents using the protocol outlined by Fisher [1]. The drugs, in their normal anaesthetic concentrations, are diluted in normal saline immediately prior to testing. Each drug is injected intradermally into the centre of an appropriately labelled area, sufficient drug being used to raise a 1–2 mm weal (0.01–0.02 ml). A control injection of saline is given to exclude dermatographism with a control injection of d-tubocurarine (1.0 ml/10 ml of saline). The latter should provoke a weal and flare response in all patients, and is used to prove

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Table 1. Drugs tested intradermally and their reactions.

Drug	Drug dose/ml of saline	Reaction at 10 min	Reaction at 40 min
Etomidate	20 μg	zero	zero
Thiopentone	250 μg	zero	zero
Propofol	100 μg	8 mm+flare	10 mm
Lignocaine	1 μg	4 mm	zero
Suxamethonium	500 μg	zero	zero
d-tubocurarine	100 μg	8 mm+flare	5 mm
Atracurium	10 μg	4 mm	zero
Vecuronium	20 μg	zero	zero
Alcuronium	50 μg	5 mm+flare	5 mm
Pancuronium	20 μg	3 mm	zero
Morphine	1 μg	5 mm+flare	zero
Saline		zero	zero

immune responsiveness. Narcotics are difficult to test as they are potent causes of false-positive results. The drugs used for premedication were not included as the reaction occurred after induction of anaesthesia. A positive reaction is one in which a weal of greater than 7.0 mm arises within 10 min and persists for at least 30 min.

The results and drugs tested are shown in Table 1. The reaction to propofol was positive. The patient was advised to wear a medic-alert bracelet and the Committee on Safety of Medicines was informed.

Discussion

Anaphylaxis has an estimated frequency of between 1:4500 and 1:20000 during general anaesthesia [2, 3], with a mortality of 1:40000 [2]. In the United Kingdom there may be between 175 and 770 severe reactions each year [4]. Three hundred and twenty-seven patients who had experienced anaphylaxis during anaesthesia were tested at a unit in France between 1984 and 1990; muscle relaxants were implicated in 77% of the cases and hypnotics (thiopentone, propofol, midazolam, and diazepam) in 6.4%. Propofol was considered the causative agent in only three of the cases. Each case was investigated using cutaneous testing, drug-specific IgE antibodies and leucocyte histamine release tests and two of these needed to be positive to confirm anaphylaxis [5]. Laxenaire *et al.* report propofol anaphylaxis in four patients with no previous history of exposure to the agent [6]. In two patients positive results were found for skin tests, leucocyte histamine liberation and propofol-specific IgE. One patient had a positive result for the human basophil degranulation test and propofol-specific IgE, and the other had a positive result for propofol-specific IgE only. Another report is of a 72-year-old patient who developed a generalised urticaria and cardiovascular collapse following induction of general anaesthesia with propofol. A positive prick test, radio-allergosorbent test (RAST) and leucocyte histamine release test established propofol as the responsible agent [7]. A further case is reported from France, of a 66-year-old man who developed anaphylaxis after propofol and who subsequently, on skin testing, gave a wheal and flare reaction, and also a positive histamine release test to propofol [8].

Intradermal skin tests are the most readily available and generally useful diagnostic test for drug allergy, and their use enables clinically useful conclusions to be made in the majority of cases of drug allergy [9]. It is a simple test requiring little expertise and reliable if carried out within 3 months of the reaction. However, although it is drug specific, it does not enable the mechanism of the reactions to be determined.

The positive results we obtained could have been caused by either 2,6 di-isopropylphenol or the intralipid solution in which it is solubilised. We did not test the patient for sensitivity to intralipid when we performed the intradermal tests, as we did not know that he would be sensitive to Diprivan. Fisher [1] does not separately test additives, vehicles, antioxidants or preservatives, with the exception of Cremophor. Our aim in testing this patient was to determine to which proprietary preparation of anaesthetic agent he was sensitive. The patient would need to avoid Diprivan whether the anaphylactoid response had been caused by 2,6 di-isopropylphenol or intralipid.

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APPARATUS

Anaesthetic machine checking practices

A survey

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Summary

Forty anaesthetists, of all grades, were interviewed without prior warning and questioned about the checks they had performed on their anaesthetic equipment before use. The results reveal that a substantial percentage (up to 41%) of anaesthetists perform inadequate checks. Furthermore, of those that do, few follow the Association of Anaesthetists of Great Britain and Ireland's recent guidelines.

Key words

Equipment; anaesthetic machines.

The Association of Anaesthetists in July 1990 recommended a procedure for the pre-operative checking of anaesthetic machines incorporating the use of a calibrated oxygen analyser [1]. This document states that improvements in safety must be an important goal in anaesthetic practice and that an important aspect of safety is the checking of equipment before use.

Craig and Wilson's survey of anaesthetic misadventures in 1981 [2] showed that failure to perform equipment checks was an associated factor in one third of the 81 misadventures. Subsequently, Cooper and coworkers [3] studied 1089 critical incidents and showed that in 20% of cases failure to check equipment was an associated factor [3]. More recently a study of 549 reported significant observations (critical incidents) over an 18 month period showed that 119 (22%) were associated with failure to check equipment [4].

We decided therefore to survey the anaesthetic machine checking practices of anaesthetists of all grades in three hospitals in our area.

Method

Forty anaesthetists of varying experience from three hospitals were interviewed during or shortly after an elective operating list. They were asked about the checks which they had performed on their anaesthetic equipment both in the anaesthetic room (AR) and in the operating theatre (OT). They were also questioned about checks performed by their assistant and to what extent these were relied upon. The anaesthetists were then asked if they had read the Association of Anaesthetists' guidelines for checking anaesthetic equipment and whether or not they felt that these pre-operative routines improved safety. Comments were also invited.

The interview was carried out by one of the authors (A.H.M. or J.M.E.) and a standard anonymous questionnaire was followed, based on the Association of Anaesthetists' guidelines [1], (Fig. 1). No anaesthetist declined to take part in the study.

Results

The results of the 40 questionnaires were analysed. No anaesthetist performed a full check as recommended in the guidelines of the Association of Anaesthetists [1]. However, in five cases the only lapse was failure to calibrate and use an oxygen analyser. If this was the only deviation from the guidelines the check was classified as 'comprehensive'. Less thorough checks were classified as 'partial', and a third group who performed no checks were classified as 'none'. Of the 40 anaesthetists interviewed 21 were Consultants, eight Senior Registrars and 11 Registrars or SHOs.

Forty-one percent of the anaesthetists questioned performed no checks on either their machine or anaesthetic equipment in the AR and 30% performed none in the OT (Tables 1(a) and (b)). Of those that did, 49% and 58% performed only partial checks and 10% and 13% performed comprehensive checks in the AR and OT respectively.

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Grade of anaesthetist interviewed ....

1. Did you perform any check on your anaesthetic machine/ equipment at the beginning of this list?
   Anaesthetic Room: Yes ...... No ......
   Operating Theatre: Yes ..... No ......
2. Did you use an oxygen analyser; Yes ...... No ......
   If Yes, did you calibrate it? Yes ...... No ......
3. Medical gas supplies:
   (a) Did you perform any checks on the pipelines?
   If Yes, which checks?
   (b) Did you perform any checks on the cylinders?
   If Yes, which checks?
   (c) Do you have a carbon dioxide cylinder on your machine?
   If Yes, did you perform any checks on it?
4. Did you check the Rotameters? Yes ..... No .....
   If Yes, which checks?
5. Did you check the function of the oxygen failure protection device? Yes ...... No ......
   If Yes, which checks?
6. Did you check the oxygen flush device? Yes ...... No ......
7. Did you check the pressure relief valve? Yes ...... No ....
8. Did you perform any checks on the vaporisers? Yes ...... No .....
   If Yes, which checks?
9. Which breathing systems did you use and which checks did you perform on them:
   Anaesthetic Theatre .... Operating Theatre ....
10. Did you check the normal operation of your ventilator and it's controls? Yes ...... No .....
11. Did you check the ventilator disconnect alarm? Yes ...... No ......
12. Did you check the suction equipment? Yes ...... No .....
    If Yes, which checks?
13. Did you check the function of a laryngoscope? Yes ...... No ......
    Have you checked a spare (second) laryngoscope?
14. Did you perform any checks between cases? Yes ..... No .....
15. Do you know what checks are performed by your anaesthetic assistant?
    No idea ....
    Vague idea ....
    Detailed knowledge of checks ....
16. How much do you rely on checks of others?
    Not at all ....
    Partially ....
    Entirely ....
17. Have you read the Association of Anaesthetists' document 'Checklist for anaesthetic machines' published July 1990?
18. Do you think these exhaustive tests as mentioned:
    (i) improve safety?
    (ii) are feasible to carry out personally?
19. Any comments?

Fig. 1. Questionnaire.

Table 1(a). Anaesthetic room checks performed. Number (%) of anaesthetists.

Group/level of check	Comprehensive	Partial	None
Consultants ($n = 21$)	2 (10)	8 (38)	11 (52)
Senior registrars ($n = 7$*)	1 (14)	4 (57)	2 (29)
Registrars/senior house officers ($n = 11$)	1 (9)	7 (64)	3 (27)
Total ($n = 39$)	4 (10)	19 (49)	16 (41)

*One of the eight SRs did not use the anaesthetic room.

Table 1(b) Operating theatre checks performed. Number (%) of anaesthetists.

Group/level of check	Comprehensive	Partial	None
Consultants ($n = 21$)	2 (10)	11 (52)	8 (38)
Senior registrars ($n = 8$)	2 (25)	6 (75)	0
Registrars/senior house officers ($n = 11$)	1 (9)	6 (55)	4 (36)
Total ($n = 40$)	5 (13)	23 (57)	12 (30)

Table 2. Summary of checks performed in 'partial check' group ($n = 23$). Number (%) of anaesthetists.

Check performed	Yes fully	Not at all/inadequately
Gas pipelines	5 (22)	18 (78)
Gas cylinders (O_2/N_2O)	2 (9)	21 (91)
CO_2 cylinders	1 (4)	22 (96)
Rotameters	3 (13)	20 (87)
Oxygen failure	7 (30)	16 (70)
Oxygen flush	17 (74)	6 (26)
Pressure relief	10 (44)	13 (56)
Vaporizer	4 (17)	19 (83)
Breathing system (operating theatre)	12 (52)	11 (48)
Breathing system (anaesthetic room)	12 (52)	11 (48)
Ventilator	11 (48)	12 (52)
Ventilator disconnect alarm	4 (17)	19 (83)
Suction equipment	12 (52)	11 (48)
Laryngoscopes × 1	9 (39)	9 (39)
Laryngoscopes × 2	5 (22)	

Table 3. Did you perform any checks between cases? Number (%) of anaesthetists.

Grade	Yes	No
Consultant (*n* = 21)	2 (9)	19 (91)
Senior registrar (*n* = 8)	2 (25)	6 (75)
Registrar/senior house officer (*n* = 11)	1 (9)	10 (91)
Total	5 (12.5)	35 (87.5)

Only one anaesthetist questioned calibrated an oxygen analyser, although it was not then used for subsequent checks. Ten percent of those questioned used an oxygen analyser as part of their checking procedure. Fourteen percent of consultants, 9% of registrars/SHOs and no senior registrars used an oxygen analyser.

The results of the further analysis of the group of 23 anaesthetists who performed partial checks are summarised in Table 2. These reveal that gas pipelines, cylinders, Rotameters, vaporizers and ventilator disconnect alarms were rarely checked. Of those anaesthetists that did perform partial checks, most were happy provided that they had a means by which to inflate the patients lungs with what they believed to be 100% oxygen. Checking of equipment between cases was performed by 12.5% overall (Table 3). Twenty percent of anaesthetists relied entirely on their assistants to perform checks, 60% relied partially and 20% did not rely at all on others, (Table 4). Only a quarter of anaesthetists had detailed knowledge of the checks which their assistants had carried out, the rest having only a vague idea or none at all.

The majority (90%) had read the Association of Anaesthetists guidelines [1] and most (82.5%) felt that these would improve safety. However, only 70% felt that these checks were feasible.

Discussion

The results demonstrate that the standard of checking of anaesthetic equipment before use is poor. Although most anaesthetists questioned (90%) had read the Association of Anaesthetists guidelines for checking anaesthetic machines and most believed that these could improve safety few put the recommendations into everyday practice.

Nearly one third of all the anaesthetists questioned performed no checks at all in the operating theatre and 40% performed no checks in the anaesthetic room. The highest incidence of failure to check was in the consultant group, (38% in the OT and 52% in the AR) although perhaps not surprisingly anaesthetists in training also failed to perform adequate checks. Nobody interviewed used a properly calibrated oxygen analyser.

We feel that this survey raises some very important issues which must be addressed. Firstly, does it matter if we do not check our anaesthetic equipment before use? The evidence would suggest that it probably does. Several studies have shown that failure to check equipment adequately is a major factor in the occurrence of critical incidents [2–4]. Furthermore, 82.5% of anaesthetists questioned in our survey believed that pre-operative checks improve safety.

If we accept that checks should be performed, who should perform them? Should it be the anaesthetist responsible for the list or could the task be delegated to a suitably qualified assistant, either an ODA or an anaesthetic nurse? If an assistant performs the checks clearly the anaesthetist takes responsibility for any mishap. It has been traditionally accepted that the anaesthetist should both perform the checks and accept responsibility for any mishap that may occur as a result of inadequate checking. However, it could be argued that since a large proportion of anaesthetists do not appear to check their equipment adequately, more diligent anaesthetic assistants (ODAs and nurses) might undertake these tasks. With adequate training, only time and the ability to adhere to a strict protocol are required.

If anaesthetists are to perform the checks according to the Association's guidelines then additional time must be allocated both at the start of the operating list (probably about 20 min) and between cases (possibly a further 5 min). Is this realistic? It would, however, mean improved training and motivation of staff in checking procedures and use of equipment. It was worrying when one of the SHOs commented, 'I did not check the machine as I would not have a clue where to start.' In this instance the machine was a Draeger Narkomed II, an awesome machine to tackle if inadequate training has been given.

Perhaps a compromise is needed in the form of a protocol which is as safe but quicker and easier to perform than that recommended by the Association. Better compliance could itself improve safety. Whatever the checking scheme, there is no doubt that if acceptable standards of safety are to be maintained, all anaesthetists in training should receive comprehensive instruction in the use and checking procedures of all the equipment they use.

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Table 4. How much do you rely on others to check machine? Number (%) of anaesthetists.

Grade	Not at all	Partially	Entirely
Consultants (*n* = 21)	4 (19)	13 (62)	4 (19)
Senior registrar (*n* = 8)	3 (37)	4 (50)	1 (13)
Registrar/senior house officer (*n* = 11)	1 (9)	7 (64)	3 (27)
Total	8 (20)	24 (60)	8 (20)

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APPARATUS

Evaluation of the Level 1 Hotline blood warmer

J. M. B. SMALLMAN AND M. MORGAN

Summary

The Level 1 Hotline warmer is a new type of fluid warmer, developed specifically for use with low flows. It was found to be effective at flows between 1 ml.min^{-1} and 75 ml.min^{-1}.

Keywords

Equipment; blood warmer.

Hypothermia is a well documented problem in patients during major surgery and this may be exacerbated by the intravenous infusion of cold fluids. Efficient blood warmers are available to warm blood at high flows [1] but at low flows of less than 50 ml.min^{-1}, the temperature of the fluid reaching the patient falls because of heat loss along the tubing.

The Level 1 Hotline is a new type of warmer, specifically designed for flows of less than 75 ml.min^{-1}. The present study investigated the efficiency of this fluid warmer in a laboratory setting.

Apparatus

The Level 1 Hotline consists of two components, the fluid heater/reservoir and the disposable giving set.

Hardware (Fig. 1(a) and (b))

The warming unit is easily portable and can be attached to an infusion stand. The unit has a closed reservoir which is filled with 1.4 l distilled water the level of which should be maintained between the two guide lines. The warming capacity of the unit is 300 W, which is used to heat the water to a temperature of 40°C; from 18°C it takes 8 min to achieve this. The water is then circulated through the disposable plastic tubing. There is a single on/off switch and an indicator light shows that the unit is functional. The temperature of the water is displayed on the front of the unit. Alarm lights indicate if the water level is too low, if the water is overheating or if the disposables are not correctly set up.

Disposable giving set

This consists of a 245 cm length of soft plastic tubing with connectors at each end, and incorporates an air eliminator at the patient end to eliminate microbubbles. The connector for the warmer has two prongs to fit into the warmer and a Luer lock port that will attach to any giving set. The patient end has a Luer lock to attach to any cannula inserted into the patient.

The tubing has a central lumen, internal diameter 3.0 mm, surrounded by an outer layer through which the warm water circulates down one side and then back up to the reservoir. (Fig. 2). The priming volume is 19 ml.

The Fenwal warmer was used for comparison since it is the one commonly used in this department.

Method

Saline 0.9% at 4°C and 18°C was passed through the Level 1 Hotline and the Fenwal, at flows varying from 1 ml.min^{-1} to 125 ml.min^{-1}. The saline used had either been refrigerated overnight to chill to 4°C (range 4–6°C), or taken from a cool store room at 18°C. The temperature of each bag was measured by inserting the thermistor thermometer into the fluid. The constant flows were provided by an IMED 960A pump for flows between 1 ml.min^{-1} and 16 ml.min^{-1} and an American Optical Roller pump for flows between 16 ml.min^{-1} and 125 ml.min^{-1}. The flows were determined by collecting the fluid issuing from the Hotline in a measuring cylinder over 5 min.

The outflow temperature was measured using a Yellow Springs Instrument Co. series 401 thermistor thermometer

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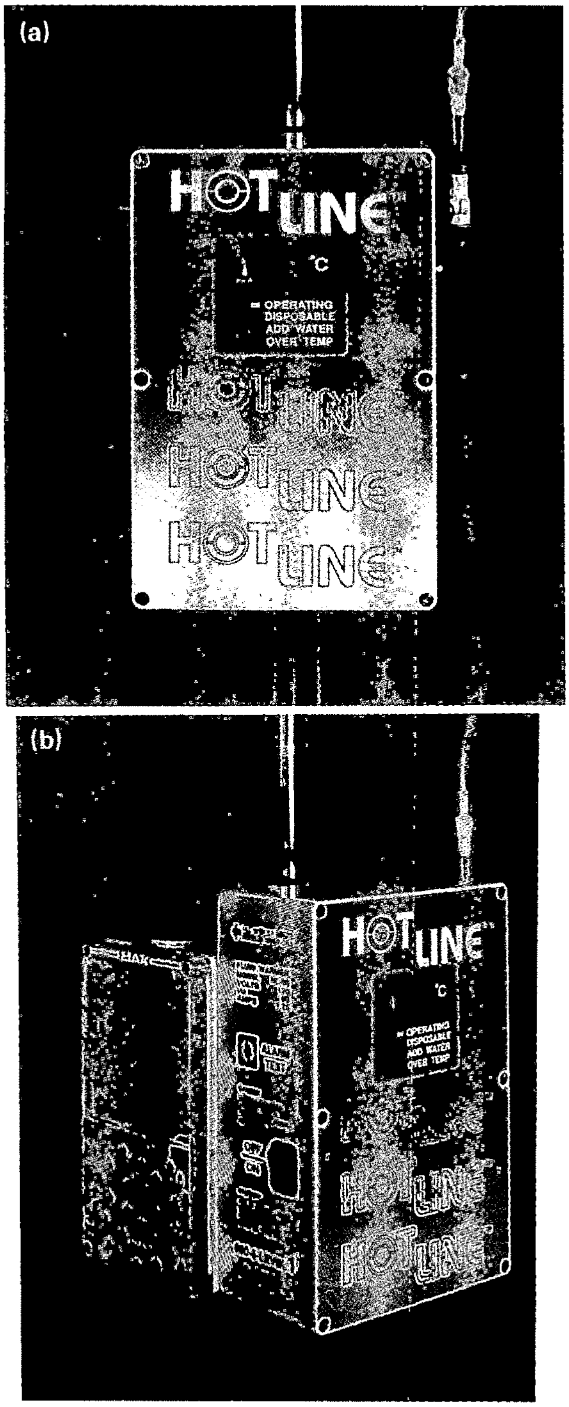

Fig. 1. The Hotline blood warmer. The connector for the 'warming' tubing and the infusion set is situated at the top right of the warmer.

which had been calibrated against a National Physical Laboratories calibrated mercury in glass thermometer. Using a Y-connector, the thermistor was held in the flow of saline in such a way that it did not obstruct the flow. The outflow temperature was measured after 38 ml of fluid (2 × priming volume) at each particular flow had run through the warmer. The temperature of the issuing fluid and the flows were measured on three occasions.

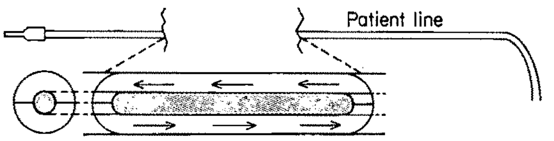

Fig. 2. The 'warming' tubing, showing the flow of warm water surrounding the infusate. →, water circulating at 40°C; shaded area, blood or solution warming path.

Results

The results obtained are shown in Figures 3 and 4. There was no significant variation when the measurements were repeated. At flows of less than 55 ml.min^{-1}, the Level 1 Hotline warmed fluid more effectively than the Fenwal warmer, regardless of the input temperature. The Fenwal failed to warm fluid to above 34°C at any flow, whereas the Hotline warmed fluid from 4°C to above 34°C at a flow of 55 ml.min^{-1} and from 18°C (the temperature likely to be found in fluids from the store room) to above 34°C at a flow of 75 ml.min^{-1}. As the flow increased, the difference between the Hotline and the Fenwal decreased, particularly with an initial temperature of 4°C and a flow of 76 ml.min^{-1}, at which point the performance of the Fenwal was superior to that of the Hotline.

Discussion

The temperature of fluid entering the patient is lower than that at which it leaves a blood warmer because of heat loss from the tubing connecting the warmer and the patient [2].

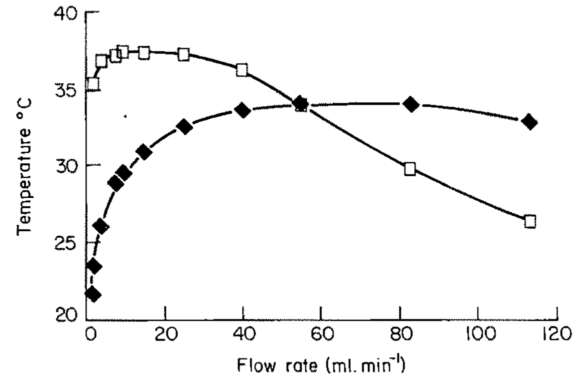

Fig. 3. Relationship between flow and issuing temperature using the Hotline (□) and Fenwal (◆) warmer. The temperature of the fluid entering the warmer was 4°C.

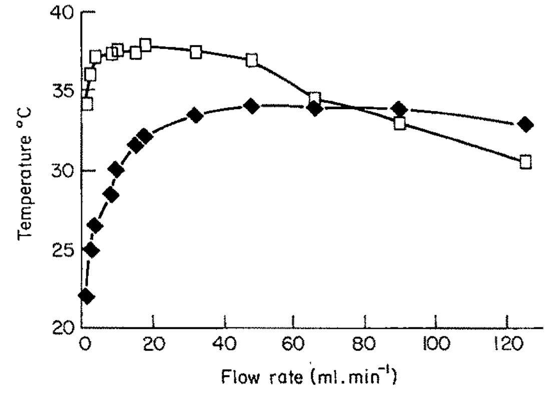

Fig. 4. Relationship between flow and issuing temperature using the Hotline (□) and Fenwal (◆) warmer. The temperature of the fluid entering the warmer was 18°C.

Attempts have been made to insulate the extension tubing, but with little success [3]. The Level 1 Hotline blood warmer avoids this problem by using the tubing between the warming unit and the patient to warm the intravenous fluid. This is particularly efficient at low flows, from 1–50 ml.min^{-1} (60-3000 ml.h^{-1}).

All patients undergoing surgery lose heat through a number of mechanisms and attempts should be made to minimise these losses. Intravenous fluids are administered at operation, not only to replace the circulating blood volume, but also to replace deficits and slow continuous losses as a result of pre-operative reduction in fluid intake, fluid shifts due to surgery and evaporation; such replacement is particularly important during prolonged surgery. The heat required to warm these relatively small, low flow infusions is usually ignored and the warmers currently available are too inefficient at such flows to make them worth using. However, the specific heat of water is 4.186 kJ.kg^{-1}.K^{-1} and that of whole blood is 3.642 kJ.kg^{-1}.K^{-1}. Therefore to heat 1 l of crystalloid from 18°C to 37°C requires 79.53 kJ. To heat 1 l of blood from 4°C to 37°C, would take 120 kJ. This would correspond to a fall in core temperature of 0.5°C [4]. This is usually a clinically insignificant amount, but repeated with several litres of crystalloid over several hours might result in a significant fall in core temperature of the patient. This heat loss is particularly relevant in the young, the elderly and the malnourished. Children are already at a greater risk of a decrease in core temperature because of their large surface area to weight ratio and the elderly have impaired metabolic responses to meet this demand. The malnourished patient has impaired thermoregulation [5] and is therefore also susceptible to hypothermia. Such patients are less able to make up heat by increasing metabolism postoperatively, so that they spend longer in recovery before returning to the wards.

Mortality has been shown to increase in trauma [6] and general surgical patients [7] when there is a fall in core temperature. The effect of cold postoperatively is marked. Vasoconstriction occurs at 36°C, leading to an increase in cardiac afterload and shivering produces an increase in oxygen consumption. As the core temperature continues to decrease, platelet function is impaired and the oxygen dissociation curve shifts to the left, thus reducing oxygen delivery to the tissues. It is therefore important in the high risk patient to try to minimise these effects.

The apparatus described effectively warms intravenous fluids given at slow rates and it would have an important rôle in those patients requiring slow, but steady, replacement.

Acknowledgment

We thank Mr R. Penberthy of Pennco Medical Ltd for supplying the Level 1 Hotline warmer.

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Anaesthesia, 1992, Volume 47, pages 872–877

APPARATUS

The Extensometer — use in spontaneously ventilating awake volunteers

J. BRIMACOMBE, A. MACFIE AND A. MASTERS

Summary

The extensometer is a new device with potential in the field of respiratory pattern analysis. This paper describes the physical principles upon which the extensometer depends and also assesses its performance as a noninvasive respiratory monitor in respect of its ability to measure tidal volume and to determine obstructive breathing patterns in awake volunteers in the supine position over a limited time period. Further developments of the device are outlined and the current status of torso transducers in anaesthesia and intensive care are discussed.

Key words

Measurement techniques; extensometer
Monitoring; ventilation.

The extensometer is a new device with several potential applications in anaesthesia and intensive care, particularly in the field of respiratory pattern analysis [1]. The basic functions and the initial laboratory testing of the device have already been described [1, 2]. It comprises a length of silicone rubber which incorporates two wires coiled almost like a double helix (Fig. 1). When stretched it behaves like a variable parallel plate capacitor with a stray capacitance term.

$$C = C(x) + C^{\sim} \qquad (1)$$

Total capacitance (C) is equal to the capacitance of the length x, C(x), plus the stray capacitance term $C^{\sim}$.

$$C(x) = \frac{k}{(x_0 + dx)} \qquad (2)$$

The capacitance of length x is equal to a constant k divided by the total length (original length x_0 plus stretch dx).

$$f(x) = \frac{h}{C} \qquad (3)$$

If the extensometer is included in a simple oscillator circuit, the resulting frequency at length x, f(x), is related inversely to the total capacitance (C) and directly to a constant h.

$$f(x) = m\,(x_0 + dx) \qquad (4)$$

It follows therefore that the frequency at any length, f(x), is directly proportional to the total length $(x_0 + dx)$ multiplied by a constant m.

The analogue frequency signal produced is processed through a signal conditioning unit and can be converted into a voltage output or can be fed directly into a computer, thus avoiding the need for a DC/analogue converter. In addition, the oscillator can drive a small FM transmitter directly and the detected signal can be demodulated using the same signal conditioning unit. Finally, the sensitivity of the device can be altered by adjusting an offset switch (Alberto Cimmino, personal communication).

The previous study [1] demonstrated the use of the extensometer in patients whose lungs were being ventilated. This study was designed to assess the use of the extensometer as a torso transducer in awake volunteers and to determine whether it was capable of estimating tidal volume after calibration against a spirometer. Its ability to distinguish between totally obstructed and unobstructed breathing was also assessed.

Methods

Thirty-eight healthy volunteers participated in the clinical study. The volunteers were in the supine position and breathed through a circuit with a one-way valve. An Ohmeda 5400 tidal volume monitor (accurate to within 8% according to the manufacturer's specifications) was incor-

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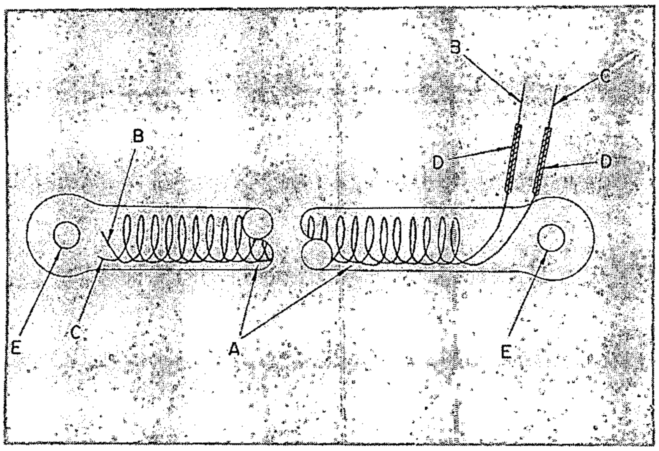

Fig. 1. A schematic representation of the extensometer. A, wires coiled in silicone rubber (60 coils cm^{-1}); B and C, separate wires; D, insulation; E, hooks for attachment.

porated into the expiratory side of the valve to record expired tidal volume. Breathing was through a mouth piece with a nose clip in position.

The extensometers were connected anteriorly to rigid fabric bands which had been placed around most of the volunteer's rib cage (RC) and abdomen (AB) at the level of the fourth rib in the midclavicular line and the level of the umbilicus respectively [1]. The extensometers were connected to a voltmeter and a multichannel chart recorder. Each extensometer was stretched to 107.5% of its original length (as determined by laboratory testing) when the volunteers were at functional residual capacity (FRC), and were not adjusted after being placed in position. When the volunteers were familiar with breathing through the system they were asked to perform four breathing manoeuvres. Normal resting tidal breathing was maintained for 20 breaths (NRTB). A 'various tidal volume manoeuvre' (VTVM) was performed, in which the volunteers were instructed to start breathing shallowly and then gradually to increase their tidal volume until they were breathing at near vital capacity. Once maximal tidal volume had been reached they were instructed to reduce tidal volume gradually until they were breathing shallowly again. All volunteers were asked to return to FRC at the end of each breath. An obstructed breathing manoeuvre (OBM) was conducted, starting at FRC and with the airway totally obstructed. The OBM started off at imagined normal tidal volumes (i.e. isovolume manoeuvres) and then gradually built up in effort for as long as tolerable. Finally, an isovolume manoeuvre (IVM) was performed, starting at FRC, in which the airway was again totally obstructed. The volunteers were asked to breathe at imagined normal tidal volumes for 30 s. During OBM and IVM, the airway was obstructed with a nose clip and the mouth shut tightly. A period of practice and rest was allowed before the formal recording of each manoeuvre.

The change in voltage output for each waveform during NRTB and VTVM was measured from the hard copy during each breath for chest (RC_v) and abdomen (AB_v), and a value for chest plus abdomen (RC_v+AB_v) was derived. The peak voltage output of each waveform during VTVM was converted into peak length changes using the calibration data obtained during previously published laboratory testing [1]. Data were obtained for circumference changes during each breath for RC and AB, and a value for RC+AB was derived. Values were also obtained for the ratio of chest to abdominal wall movement during VTVM for each breath and a mean derived for each volunteer.

The maximum and minimum peak voltage changes during OBM from the FRC baseline were determined and a ratio for chest and abdominal wall movement was derived for each obstructed breath effort. Thus, an average value for this ratio was determined for each volunteer.

The maximum and minimum voltages obtained during IVM were also measured for each breath effort and an average ratio between RC_v and AB_v (K) derived in accordance with the Konno-Mead principle [3], K being the proportionality factor which allows chest and abdominal movement to be balanced.

$$K = -AB_v/RC_v \tag{5}$$

K was derived for every isovolume breath effort and the average determined. The values obtained for RC_v+AB_v during each VTVM were plotted against spirometrically measured tidal volume V_T (sp) and then underwent regression analysis without modification (the non Konno-Mead (non-KM)) group. In addition, the values for RC were multiplied by K and regression analysis performed for V_T (sp) plotted against $[(K.RC_v)+AB_v]$ (the Konno-Mead modified (KM) group. Overall r^2 values and the gradient (M) were derived for each patient for the non-KM and KM groups with the intecept forced through zero. The values of M for the non-KM group were then applied retrospectively to the NRTB measurements of RC_v+AB_v using the following formula to derive a value for calculated tidal volume (V_T (non-KM)).

$$V_T\text{ (non-KM)} = M\,(RC_v+AB_v) \tag{6}$$

In addition, the values for K and M from the KM group were applied retrospectively to NRTB measurements of RC_v and AB_v using the formula given below to derive a calculated tidal volume, V_T (KM).

$$V_T\text{ (KM)} = M\,[(KRC_v)+AB_v] \tag{7}$$

A ratio of calculated V_T to V_T (sp) was derived and converted into percentage error for each breath for the non-KM and KM groups.

The results were analysed using regression analysis and Student's *t*-test.

Results

Nineteen men and 19 women participated in the study. Demographic data are shown in Table 1. The ranges of tidal volume, and chest and abdominal wall movement, are shown in Table 2. The total number of breaths analysed during VTVM for men and women was 24.6 (SD 6.91) and 26.6 (6.28) respectively. The data from all volunteers have been included in the analysis unless stated otherwise. Examples of the VTVM and OBM hard copy are shown in Figures 2 and 3.

Mean r^2 values for the increases in circumference of RC, AB and RC+AB plotted against V_T during VTVM are shown in Table 3. The mean r^2 values of V_T plotted against RC+AB obtained during VTVM for the non-KM group was 0.951 (SD 0.049) and for V_T plotted against [(K.RC)+AB] in the KM group was 0.947 (SD 0.043)

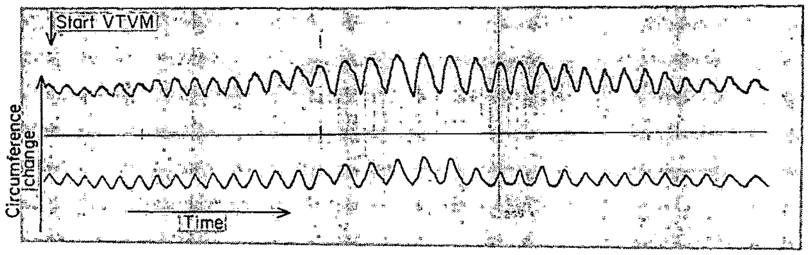

Fig. 2. An example of a variable tidal volume manoeuvre (VTVM). The top trace represents change in chest wall circumference and the lower trace change in abdominal wall circumference.

Table 1. Demographic data of volunteers.

	Age (years)	Height (cm)	Weight (kg)	Chest circumference (cm)	Abdominal circumference (cm)
Men	33.7	177.0	73.0	95.7	83.3
	(6.6)	(8.9)	(10.1)	(4.8)	(5.6)
Women	31.0	164.0	57.2	85.6	73.1
	(6.4)	(4.0)	(5.6)	(4.5)	(5.9)

Table 2. The range of tidal volume, chest and abdominal wall movement as mean (SD).

	Tidal Volume (ml)		Chest circumference change (cm)		Abdominal circumference change (cm)	
	Max	Min	Max	Min	Max	Min
Men	2907	246	2.57	0.24	2.06	0.27
	(781)	(89)	(0.61)	(0.09)	(1.12)	(0.19)
Women	1810	235	1.77	0.21	1.50	0.25
	(442)	(111)	(0.57)	(0.10)	(0.60)	(0.12)

indicating a near linear relationship for both groups. The relationship for chest plus abdomen was nearly linear for men (mean (SD) r^2 0.964 (0.032)), but less linear for women (0.937 (.046)). The r^2 values for chest (RC) and abdomen (AB) were less than those for (RC+AB) for both men and women. The relationship for RC was significantly more linear than for AB for men ($p < 0.05$), but not for women. The results for the KM group were almost identical.

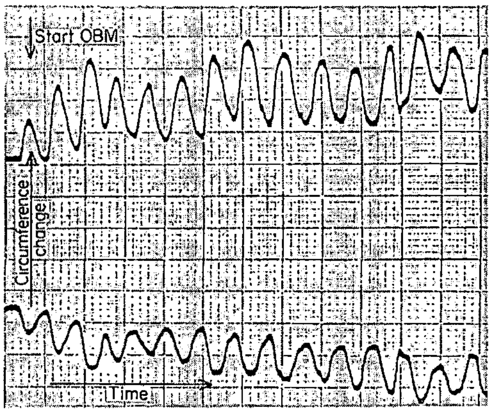

Fig. 3. An example of an obstructed breathing manoeuvre (OBM). The top trace represents chest wall movement and the lower trace abdominal wall movement.

The x coefficients for chest and abdominal wall movement with increasing V_T are shown in Table 4. Chest wall movement was significantly greater than abdominal wall movement in men ($p < 0.001$), but not in women.

Two men and three women were unable to perform

Table 3. The mean r^2 values for increase in circumference of chest, abdomen and chest plus abdomen (cm) plotted against tidal volume (ml) as mean (SD).

	r^2 Chest	r^2 Abdomen	r^2 Chest plus abdomen
Men	0.907	0.782	0.964
	(0.097)	(0.203)	(0.032)
Women	0.839	0.796	0.937
	(0.160)	(0.199)	(0.046)

Table 4. The gradient or x coefficient of chest circumference (cm) and abdominal circumference (cm) plotted against increasing tidal volume as mean (SD).

	Chest circumference change (cm.l^{-1})	Abdominal circumference change (cm.l^{-1})
Men	0.947 (0.345)	0.575 (0.261)
Women	0.917 (0.338)	0.714 (0.292)

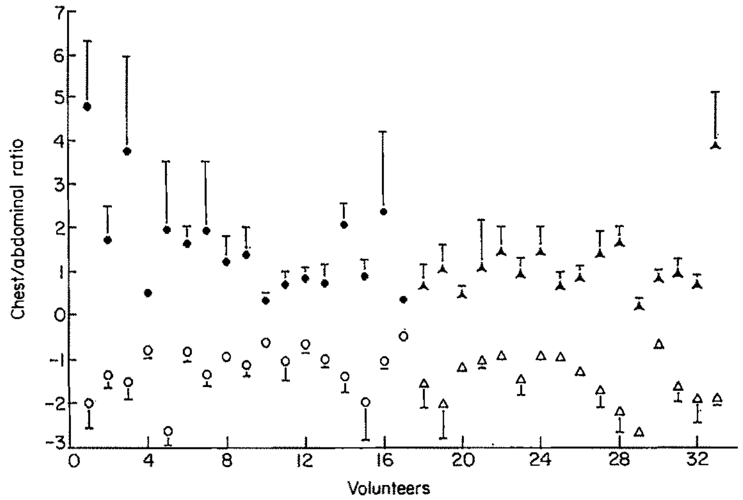

Fig. 4. Mean ratio of chest to abdominal wall movement for each volunteer during VTVM and OBM. Group 1 ○ OBM, men. Group 2 ● VTVM, men. Group 3 △ OBM, women. Group 4 ▲ VTVM, women.

Table 5. The mean changes in chest and abdominal wall circumference (cm) during the obstructed breathing manoeuvre (OBM).

	Chest circumference (cm)	Abdominal circumference (cm)	C/A*	Breath efforts**
Men	0.83	−0.78	−1.17	8.53
	(0.35)	(0.31)	(0.52)	(3.09)
Women	0.71	−0.54	−1.37	10.40
	(0.32)	(0.24)	(0.45)	(3.57)

*Mean ratio of chest/abdomen circumference change

**Number of breath efforts recorded.

OBM and IVM and their results have been excluded from subsequent analysis. The mean changes in chest and abdominal wall circumference during obstructed breathing are shown in Table 5. The mean (SD) ratio of chest to abdominal wall movement during OBM was −1.17 (0.517) for men ($n = 17$) and −1.368 (0.415) for women ($n = 16$). The mean ratio of chest to abdominal wall movement during VTVM was 1.571 (1.163) for men ($n = 19$) and 1.347 (0.918) for women ($n = 19$). Comparisons of the ratio of chest to abdominal wall movement during VTVM and OBM for each individual able to perform OBM were made using Student's t-test since the ratios were distributed normally (Fig. 4). In all individuals this was very highly significant ($p < 0.0001$).

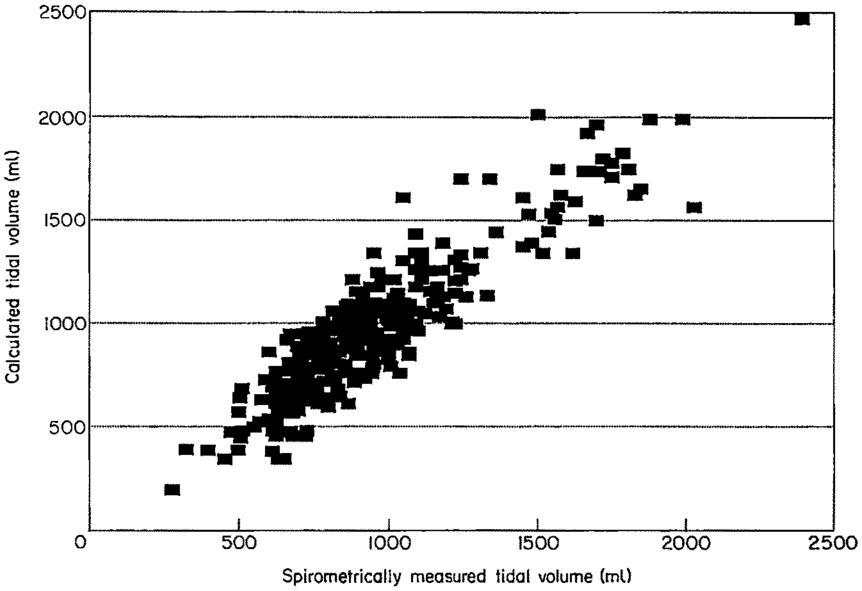

Fig. 5. A scatterplot of calculated tidal volume versus measured tidal volume for the non-KM group.

Table 6. The percentage errors for calculated and measured tidal volume for the non-KM group and KM group.

	V_T NRTB[1] mean (SD)	Error % non-KM[2] mean (SD)	Error % KM[3] mean (SD)
Men	947 (164)	3.8 (9.6)	4.1 (8.5)
Women	896 (126)	4.4 (10.4)	4.5 (9.7)
Total	940 (147)	4.1 (9.9)	4.3 (9.1)

[1] Tidal volumes during normal resting tidal breathing.
[2] Percentage error for V_T (non-KM) versus V_T by spirometry.
[3] Percentage error for V_T (KM) versus V_T by spirometry.

The mean (SD) number of isovolume breath efforts analysed to derive K for each volunteer was 9.5 (4.2). The mean value for K was 0.81 (0.45). A total of 663 spirometrically measured tidal volumes obtained during NRTB were compared to calculated tidal volumes for the non-KM and KM groups. The overall mean error for non-KM group was +4.3% (9.1) and the KM group 4.1% (9.9) (Table 6). This indicates that 96.6% of derived values were contained within an error range of +22.5% to 13.9% of V_T in the non-KM group, and +23.9% to 15.7% in the KM group (Fig. 5). Thus the application of the Konno-Mead principle made no improvement to the accuracy of the extensometer in this study.

Discussion

The first study on the extensometer in ventilated patients demonstrated that it had potential in the field of respiratory pattern analysis [1]. This follow-up study confirms that the device can be used to analyse respiratory patterns in spontaneously ventilating conscious volunteers in the supine position for a limited time period.

The relationship between changes in rib cage circumference at various lung volumes has been studied by Agostoni *et al.* [4] using mercury-in-rubber strain gauges. They demonstrated a near linear relationship, but used the sternoxiphisternal joint as their point of reference. Faithfull *et al.* [5], using four mercury-in-rubber strain gauges and a mathematical model, produced data for changes in chest and abdominal wall circumference at various tidal volumes which are similar to our findings. The x coefficients for change in chest and abdominal wall circumference show that chest circumference increases significantly more than abdominal wall circumference in men per unit tidal volume ($p < 0.001$). This difference was not significant in women, suggesting that during a VTVM, in terms of changing circumference, men breathe predominantly with their chest and women show no preference.

Comparison of the ratios of chest to abdominal wall movement during the VTVM and OBM showed highly significant differences and demonstrate that the extensometer might be able to diagnose obstructive apnoea. The data demonstrate also that a close approximation of spirometrically measured resting tidal volume can be obtained from the extensometer with or without modification by the Konno-Mead principle. These figures compare favourably with those obtained for the Respiratory Inductive Plethysmograph in the supine position using a variety of other calibration techniques [6, 7]. It is interesting that the application of the Konno-Mead principle did not significantly improve the ability of the extensometer to predict V_T. This may have been due to inadequate training of the subjects, or due to the accurate results obtained without calibration.

The calibration, and hence improved accuracy, of most noninvasive respiratory monitoring devices depends on the approximation that the respiratory system behaves like a simple physical system moving homogeneously with two degrees of freedom such that the volume change at the mouth is equal to the sum of the volume changes of the chest and abdomen [3]. When the airway is occluded, the system has only one degree of freedom and any change in RC and AB must be equal and opposite. Performance of an isovolume manoeuvre at FRC allows the gains on the RC and AB transducers to be appropriately proportioned, leading to increased accuracy of the device. There are a wide variety of calibration procedures including the isovolume manoeuvre procedure [3], the simultaneous equation method [8] and the least squares method [7]. Alternative methods are still being described [6]. Following calibration, volumetric accuracy, timing and proportionality are validated through a variety of breathing manoeuvres [9].

It may be possible to improve the accuracy of the extensometer as a predictor of V_T by more vigorous application of the Konno-Mead principle or by using different calibration techniques or more extensometers, or by taking into account other changes in torso dimensions which occur during respiration [5, 10].

Further studies using alternative calibration techniques are required to determine which calibration method is best and whether or not the Konno-Mead principle is required to improve results. The performance of the IVM usually requires training and is difficult to reproduce in patients [9]. Any noninvasive respiratory monitor which can provide accurate results without the need for complex calibration techniques is clearly at an advantage. Studies involving different positions, body types and disease states are also required before direct comparisons can be made with other noninvasive respiratory monitoring devices. In addition, the use of the extensometer for prolonged respiratory pattern analysis has yet to be determined. Such studies require the development of a computer-driven data acquisition and analysis system that can make use of the highly sensitive output from the extensometer and record data for prolonged periods. The design and testing of such a system is in progress.

The science of noninvasive respiratory monitoring has made many advances in the last 10 years. These devices have been shown to be not just research tools, but to be useful in clinical decision-making [9]. There are many devices capable of being used as torso transducers [11], but only Respiratory Inductive Plethysmography has been developed into a useful clinical instrument [9]; it can be used to analyse complex respiratory patterns and as a guide to more successful weaning and monitoring in the intensive care unit [12–14]. There are a number of reasons why noninvasive respiratory monitoring has not gained widespread popularity. Firstly, these devices are relatively new and knowledge of their availability limited. Secondly, their clinical limitations have not been fully outlined. Finally, high costs and the lack of information about cost-effectiveness may have prevented their widespread clinical use.

The extensometer has not yet been developed into a noninvasive respiratory monitor, but has some potential in this area because the hardware is cheap and simple and yet highly accurate and sensitive. In addition, the signal produced can be fed directly into a computer and can be converted instantly into length. The cost of developing software and dedicated hardware for the acquisition and analysis of data from the device is not known, but it is possible that the extensometer might become a more affordable noninvasive respiratory monitor and permit more widespread use of such monitoring.

Acknowledgments

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APPARATUS

An evaluation of the gum elastic bougie

Intubation times and incidence of sore throat

J. P. NOLAN AND M. E. WILSON

Summary

This study was designed to evaluate the routine use of a gum elastic bougie for tracheal intubation. The median time to intubation with the gum elastic bougie while simulating an 'epiglottis only' view was only 10 s longer than the time taken during conventional intubation with an optimum view. Three of the patients required a gum elastic bougie-assisted intubation after attempts at conventional visual intubation had failed. There was no significant difference in the incidence of postoperative sore throat and hoarseness between the two groups. We recommend that anaesthetists should use the gum elastic bougie whenever a good view of the glottis is not immediately obtained.

Key words

Intubation; gum elastic bougie.
Complications; sore throat.

Tracheal intubation is usually performed under direct vision with the Macintosh laryngoscope. In some patients, despite correct positioning of the head and neck and backward pressure on the larynx, considerable pressure may have to be exerted with the laryngoscope to achieve even a glimpse of the vocal cords. If the laryngeal aperture cannot be seen, intubation may require several attempts and may result in damaged teeth or end in failure. In these circumstances the technique of intubating over a gum elastic bougie, first described by Macintosh in 1949 [1], is often successful [2]. This has become a popular technique with British anaesthetists when intubation proves difficult. However, it might be sensible to resort to the use of a gum elastic bougie more readily if there is any difficulty whatsoever in seeing the cords. Anaesthetists might be more willing to employ this technique if it can be shown that the intubation time is not appreciably prolonged by it, and that it is not associated with unacceptable complications.

This study was designed to compare intubation times with and without the gum elastic bougie, and to establish whether or not use of the device is associated with an increase in the incidence of sore throat or hoarseness postoperatively.

Methods

Ethics committee approval was obtained. One hundred and fifty-two patients, ASA grades 1–3, who required tracheal intubation as part of the anaesthetic technique for elective surgery, were studied. Patients were either premedicated with temazepam or received no medication. Intubations were performed by the authors, both of them experienced anaesthetists. Patients less than 16 years old, and those requiring a rapid sequence induction, were not studied.

Patients were positioned in the 'sniffing' position, with one pillow under the head. Anaesthesia was induced intravenously and neuromuscular blockade was achieved with either suxamethonium 1 mg.kg^{-1} or vecuronium 0.1 mg.kg.$^{-1}$. Intubation was attempted 1 min after giving suxamethonium and 3 min after vercuronium. This provided adequate muscle relaxation for laryngoscopy in all patients. Patients' lungs were ventilated manually using a Magill breathing system. An initial laryngoscopy, with a size three Macintosh blade, was performed in order to grade the amount of larynx seen [3]. If necessary, laryngeal manipulation was used to improve the view: grade 1, at least some of the glottis can be exposed; grade 2, only the arytenoids can be exposed; grade 3, the glottis cannot be exposed, but the epiglottis can be seen; grade 4, neither the glottis nor epiglottis can be seen.

After the amount of larynx seen was classified, the laryngoscope was removed and the patient randomly allocated to either intubation under direct vision (visual group) or intubation over a 15 Ch gum elastic bougie (Eschmann Healthcare, Lancing, West Sussex, UK) (bougie group). Because the grade of laryngoscopy is the most important factor influencing the ease of intubation, patients were stratified according to grade and then randomised using a

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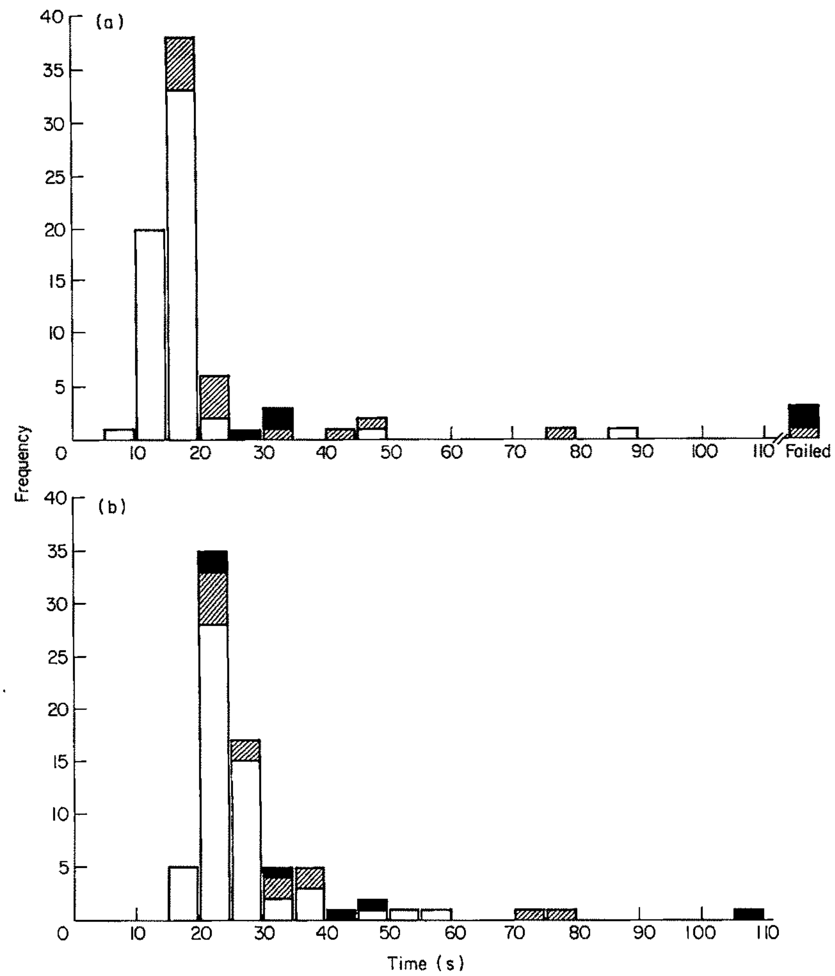

Fig. 1. (a) Intubation times for the visual group. The failures were successfully intubated with the aid of a bougie. (b) Intubation times for the bougie group when difficult intubation was simulated. Grades at initial laryngoscopy: ■, grade 3; ▨, grade 2; □, grade 1.

minimisation technique [4]. This ensured that approximately equal numbers of patients were allocated to each method of intubation for each grade of laryngoscopy.

In the visual group of patients the laryngoscope was again used to get the best view of the larynx, and the patient was intubated with a Curity (The Kendall Company, Mansfield, MA 02048, USA) cuffed tracheal tube of either 8 mm internal diameter for men or 7 mm for women. A stop watch was started the moment the anaesthetist took the laryngoscope from the assistant, and stopped when successful intubation was confirmed with Wee's oesophageal detector [5]. In the operating theatre, correct placement of the tube in the trachea was confirmed by auscultation and capnography. If intubation was unsuccessful after two attempts, a gum elastic bougie was used.

In the bougie group of patients, a stop watch was started as soon as the anaesthetist took the laryngoscope. This was used to expose the epiglottis only. A well-lubricated gum elastic bougie (15 Ch) was passed behind the epiglottis and correct placement was indicated by (a) feeling clicks as the bougie slid over tracheal rings [6,7] or (b) rotation of the bougie as it entered a main bronchus or (c) hold up of the bougie as it reached the small bronchi [6,7]. Once located in the trachea, the bougie was steadied by an assistant, and with the laryngoscope still held in the mouth, the tracheal tube was gently 'rail-roaded' over the top. Just before the tube was passed through the cords, it was rotated a quarter-turn anticlockwise, so that the bevel faced posteriorly. This manoeuvre, performed while still keeping the laryngoscope in the mouth, has been shown to improve the rate of successful first-time intubation [8–10]. The bougie was then withdrawn and, once successful tracheal intubation was confirmed with the Wee detector, the watch was stopped. Patients were interviewed the next day using a standardised interview format: (1) Was your anaesthetic alright? (2) Do you have or have you had a sore throat? (3) Do you have or have you had a hoarse voice? The patients responses to questions 2 and 3 were recorded as nil, slight, moderate, or severe.

Results

The best initial views at laryngoscopy (with backward pressure on the larynx if necessary) were grade 1 in 114 (75%) patients; grade 2 in 27 (18%) patients; grade 3 in 11 (7%) patients, and grade 4 in none of the patients.

Histograms of the times taken for intubation are displayed in Figures 1(a) and (b). The medians and ranges are presented in Table 1. Overall the visual technique is

Table 1. Intubation times.

	Number	Median (s)	Range (s)
All grades			
Visual group	74	18	10–90
Bougie group	75	28	17–110
Grade 1			
Visual group	58	17	10–90
Bougie group	56	25	17–60
Grade 2			
Visual group	13*	22	16–79
Bougie group	13	30	21–79
Grade 3			
Visual group	3†	31	27–31
Bougie group	6	32	23–110

*An additional patient was intubated with the gum elastic bougie after failing twice with the visual technique.

†An additional two patients were intubated with the gum elastic bougie after failing twice with the visual technique.

Table 2. Incidences of sore throat and hoarse voice (n = 139).

	Nil (%)	Slight (%)	Moderate (%)	Severe (%)
Sore throat				
Visual group	48 (67)	16 (22)	4 (6)	4 (6)
Bougie group	40 (60)	23 (34)	3 (4)	1 (1)
Hoarse voice				
Visual group	52 (72)	16 (22)	3 (4)	1 (1)
Bougie group	51 (76)	11 (16)	5 (7)	0

quicker (Mann–Whitney *U* test, p < 0.001). There was no appreciable difference in the median intubation times between the two anaesthetists (visual group 18 s vs 17 s, bougie group 25 s vs 26 s). Ninety percent of intubations were performed within 45 s, whichever technique was used. However, in the visual group, three patients could not be intubated despite two attempts (one laryngeal grade 2 and two grade 3), although intubation was subsequently successful in all three with the aid of the gum elastic bougie. All patients in the bougie group were successfully intubated and since in this group only the epiglottis was exposed, we were actually simulating difficult intubation [3].

Ninety-one percent of patients were followed up (Table 2). The incidence of moderate or severe sore throat in the visual group was 11.1% compared with 6.0% in the bougie group (95% confidence intervals 4.9–20.7% and 1.7–14.6% respectively). This difference is not significant (Chi-squared 0.6). The incidence of moderate or severe hoarseness was also similar, 5.6%, for the visual group and 7.5% for the bougie group, with 95% confidence intervals of 1.5–13.6% and 2.5–16.6% respectively. There were no other complaints or complications related to intubation.

Discussion

The purpose of this study was to see if there are any problems associated with the routine use of the gum elastic bougie. If none were found, this technique might be especially suitable for patients in whom there is a risk of damage to the teeth or cervical spine. We found that with only the epiglottis exposed it takes, on average, about 10 s longer than the visual method, irrespective of the initial laryngeal grade. However, one can place little reliance upon the difference in laryngeal grade 3 patients since only a few were studied. The incidence of sore throat or hoarseness did not differ from that produced by the conventional visual technique.

We found that 'clicks' and 'holdup', two signs which have been previously reported as being indicative of tracheal placement of the bougie, were very reliable [6,7]. Tracheal clicks (as the tip of the bougie bounces off tracheal rings) are more readily detected if the angle made by this distal part of the bougie is increased to about 60°. In addition, we have added a further sign; that of rotation of the bougie as it enters a main bronchus.

Once the gum elastic bougie had been correctly placed, there were no patients in whom the tracheal tube could not be railroaded into the trachea at the first attempt. This success rate probably reflects the fact that we left the laryngoscope in the mouth and rotated the tube 90° anticlockwise before passing it through the cords, recommendations that have been made in a previous study [9]. Failure rates of 25% and 52% have been quoted when the tube is not rotated [9,11]. In addition, we elected to use tracheal tubes with 'floppy cuffs', 1 mm smaller than the majority of anaesthetists would choose.

Our times include confirmation of the position of the tube using a Wee detector and these therefore are slightly longer than those previously reported [12]. The detector provided a convenient, quick endpoint to intubation, although correct placement was ultimately confirmed by capnography in all 152 patients.

Patients were directly questioned about sore throat or hoarseness; direct questioning results in a higher reported incidence than spontaneous complaint [13]. None of the patients in this study received anticholinergic premedication, which has been shown to increase the incidence of postoperative sore throat significantly [14]. Intubation over a gum elastic bougie is not associated with an increase in the incidence of postoperative sore throat or hoarseness, contrary to previous suggestions [3,15,16]. Indeed, we suggest that repeated attempts to pass a tracheal tube through a poorly visualised larynx is more likely to damage the larynx than if a gum-elastic bougie is gently used at the outset.

The conventional technique of intubation under direct vision with a Macintosh laryngoscope has its problems and we suggest that many of these can be overcome if the long gum elastic bougie is used more freely. It is difficult, if not impossible, to place an orotracheal tube correctly if the glottis cannot be seen. In our study, two patients could not be intubated for this reason. However, these two patients, and all six patients in the bougie group whose glottis could not be seen initially, were intubated without difficulty using the bougie.

Even if the glottis can be seen, it may not be possible to pass the tube because of peg teeth or missing teeth. This occurred in one patient in the visual group who required a bougie. In addition another patient in the visual group took 90 s to intubate as a result of awkward upper teeth, despite having a grade 1 laryngeal view.

Teeth are commonly damaged during attempts to see the vocal cords and pass the tube. For example, 52% of anaesthetists' reports to the Medical Defence Union of the United Kingdom relate to dental damage [17]. The risk of damage is minimised with the bougie technique, since only the epiglottis needs to be seen at laryngoscopy. It is not necessary to struggle beyond this point and risk damage to teeth and lips in order to improve the view.

It is important to be able to predict a grade 3 laryngoscopy when using the visual technique so that alternative techniques can be planned and a more experienced anaesthetist can be called to assist if necessary. Unfortunately, the methods devised to predict difficult intubation are disappointing because of poor sensitivity and specificity [18], although recently Frerk claims better results if two tests are combined [19]. If the bougie technique is used pre-operative prediction becomes less of a problem because only the epiglottis need be seen. The incidence of being unable to see the epiglottis is 0–0.44% [1,18,20,21] which is about 10 times less frequent than being unable to see the glottis. Unfortunately, it may also be difficult to predict the patient in whom there is no view of the epiglottis, since in the Oates study, two of these patients had Wilson risk-sums of 1 or less, and one was Mallampati class 1 [18].

If the bougie is seldom used, the anaesthetist and his assistant are not skilled in its use when it is most required.

Patients with suspected injuries of the cervical spine who require immediate tracheal intubation are best intubated orally with the head and neck manually stabilised in the neutral position [22,23]. In this position the vocal cords may not be clearly seen, therefore rather than attempting to extend the head, with the inherent risk of injuring the spinal cord, it seems sensible routinely to accept a grade 2 or 3 view and use the gum elastic bougie to assist intubation.

Although use of the gum elastic bougie may be increasing in the United Kingdom, it is less commonly used in the United States [24]. This may reflect a more widespread use of fibreoptic intubation in the latter country. Indeed, a recent description of a difficult intubation trolley, from the United States, listed four fibreoptic intubating scopes but did not include a single bougie [25]. The gum elastic bougie has the advantage of being considerably simpler and quicker to use [12]. When there is an unexpected difficult intubation in a patient with a compromised airway, fibreoptic intubation is likely to take too long.

In conclusion, we recommend that anaesthetists should not struggle to see the whole laryngeal aperture. If the cords are not immediately visible, a gum elastic bougie should be used.

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HISTORICAL NOTES

The Mancunian way

T. E. J. HEALY AND E. N. UN

Summary

The authors have examined early records of the administration of ether anaesthesia in Manchester and the lives of several medical men involved in these events. Charles Strange, a dentist and chemist, in a letter to the Manchester Guardian published on 14 January 1847, described a self-administration of ether for dental extraction, but George Bowring, a surgeon, subsequently claimed the first anaesthetic administered by a doctor in Manchester. The merits of these claims are discussed in the light of the circumstances surrounding these events.

Key words

History; George Bowring, Charles Strange.
Anaesthetics, volatile; diethyl ether.

Ether was used and demonstrated by William Morton, a dentist, on the 16 October 1846 [1]. The message reached Dr Francis Boott of Gower Street in London and he gave ether to Miss Lansdale for the extraction of a molar tooth on 19 December 1846 [1] 3 days after the ship, *Arcadia,* which carried the details to him in a letter from Dr Bigelow, docked in Liverpool [2].

The importance of the discovery of the anaesthetic effects of ether was confirmed by the haste with which the new knowledge spread [3,4] in a world in which communications were only just stirring. There was not long to wait for the first administration of ether anaesthesia in Manchester. The first account was published (Fig. 1) in *The Manchester Guardian* on the 14 January 1847 [5]. Charles Strange had written to *The Guardian* on 13 January describing the self-administration of ether in order that an assistant might remove one of his teeth. At the time Charles Strange was 31 years old and was listed in Slater's street guide to Manchester as a druggist and chymist [6]. His listings in the street guide from 1845 to 1852 continued to refer to him as druggist and chymist and as manufacturing chymist and wholesale druggist [7–10]. However, in the street guides from 1855 to 1869 his occupation was listed as dentist [11–16]. This leads one to assume that he was already dabbling in dentistry in addition to his chymist and druggist activities and hence his, otherwise surprising, use of ether for the extraction of one of his own teeth. Unfortunately he poisoned himself whilst in an unsound state of mind on 28 September 1870. He was aged 54 years and on his death certificate his occupation was given as dentist [17,18]. The inquest was held by E. Herferd, the Manchester coroner, on 30 September 1870 [18]. One must wonder whether or not he had become addicted to the anaesthetic vapours and died as a result of one self-administration too many, just 23 years after his first self-administration of ether. He did after all in his letter describe the sensations of breathing ether as similar to those caused by breathing laughing gas, 'to me exceedingly agreeable'.

The first administration of anaesthesia by a doctor was also reported in *The Manchester Guardian* on Wednesday, 3 February 1847 in a letter from a surgeon, Jas Bower Harrison dated 2 February 1847 [19]. He states: 'the patient, a lady of high respectability of this town, was the subject of a tumour, which her medical advisers Dr Bardsley and Mr Turner thought it prudent to have removed.'

It is interesting how times have changed, for in this letter only limited reference was made to the surgery: 'at this point Dr Bardsley requested Mr Turner to commence which he did with great alacrity, removing the tumour with a few strokes of the knife.'

It is significant that, in recognition of the dangers of anaesthesia and of the importance of an appropriate training in its use, he wrote: '. . . I should wish to caution the public against submitting themselves to the influence of ether for the minor operations, without the approval and superintendence of properly educated medical men.'

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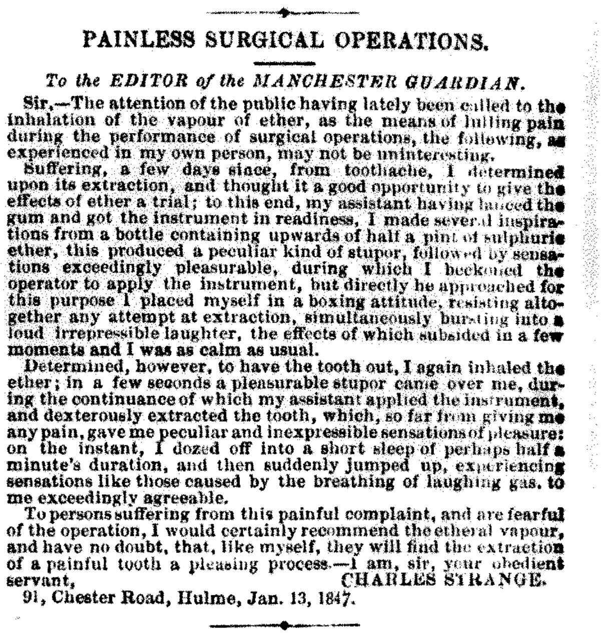

PAINLESS SURGICAL OPERATIONS.

To the EDITOR of the MANCHESTER GUARDIAN.

Sir,—The attention of the public having lately been called to the inhalation of the vapour of ether, as the means of lulling pain during the performance of surgical operations, the following, as experienced in my own person, may not be uninteresting.

Suffering, a few days since, from toothache, I determined upon its extraction, and thought it a good opportunity to give the effects of ether a trial; to this end, my assistant having lanced the gum and got the instrument in readiness, I made several inspirations from a bottle containing upwards of half a pint of sulphuric ether, this produced a peculiar kind of stupor, followed by sensations exceedingly pleasurable, during which I beckoned the operator to apply the instrument, but directly he approached for this purpose I placed myself in a boxing attitude, resisting altogether any attempt at extraction, simultaneously bursting into a loud irrepressible laughter, the effects of which subsided in a few moments and I was as calm as usual.

Determined, however, to have the tooth out, I again inhaled the ether; in a few seconds a pleasurable stupor came over me, during the continuance of which my assistant applied the instrument, and dexterously extracted the tooth, which, so far from giving me any pain, gave me peculiar and inexpressible sensations of pleasure: on the instant, I dozed off into a short sleep of perhaps half a minute's duration, and then suddenly jumped up, experiencing sensations like those caused by the breathing of laughing gas, to me exceedingly agreeable.

To persons suffering from this painful complaint, and are fearful of the operation, I would certainly recommend the etheral vapour, and have no doubt, that, like myself, they will find the extraction of a painful tooth a pleasing process.—I am, sir, your obedient servant,
CHARLES STRANGE.

91, Chester Road, Hulme, Jan. 13, 1847.

Fig. 1. Letter which appeared in *The Manchester Guardian* dated 14 January 1847.

Most of the letter was devoted to a description of the condition of the patient and her behaviour during and after the surgery, with special consideration to the effects of ether. A valuable comment, for our purpose, was made in the last paragraph: 'the apparatus used on this occasion was that invented by Dr Boott and Mr Robinson and appears to have accomplished its purpose very efficiently. It was furnished by Mr Wood, the surgical instrument maker, of King Street, who kindly attended with the instrument, and with the aid and superintendence of Mr Bowring, the house surgeon of the infirmary, regulated the inhalation of ether. I am informed by Dr Bardsley, who consulted his watch at the time, that the effects of the ether lasted four minutes and a half. He has since politely written to inform me that the lady is doing well. I have the honour to be Sir, your obedient servant, Jas Bower Harrison, Surgeon.'

It is interesting that, in a letter dated 4 February published in *The Manchester Guardian* on 6 February 1847 [20], John Braithwaite, a surgeon at the Royal Infirmary, drew particular attention to the comment in Mr Harrison's letter in which the public were cautioned against submitting to the influence of so potent an agent without the advice and superintendence of properly educated medical men. Mr Braithwaite recommended clinical evaluation of ether: 'we want to know whether it has been supposed or found to interfere with the chance of recovery after the most important surgical operation in which it has been used. This is of the utmost importance to know but difficult to be known, and it were well if the progress and termination of each case could be given. Such trials as have yet been made in the Infirmary, in cases of important operations, have been so incomplete and unsatisfactory in their nature, that it would be difficult to draw correct inference from them, as only one patient could be said to have been fairly under its influence, . . .'

We may be sure that the thoughts expressed by this surgeon in Manchester were little different from those expressed by others who were experimenting in the use of ether to provide pain free surgery in other parts of the country. The surgeons of the day recognised the need for appropriate clinical trials. They also recognised that the administration of anaesthesia demanded special skills and that only those medical men who had these skills should administer ether.

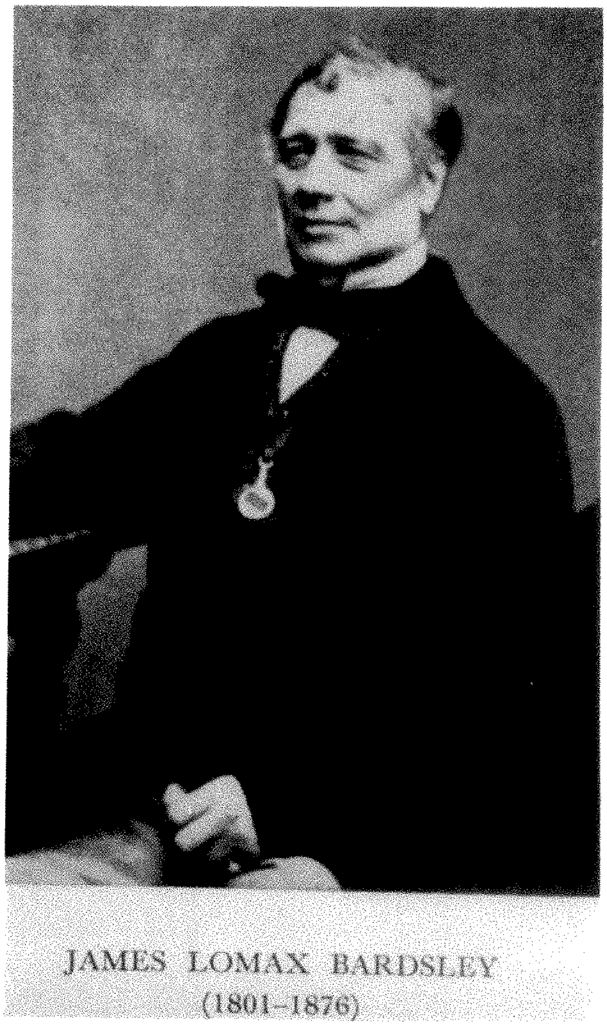

Fig. 2. Dr James Lomax Bardsley. Distinguished Physician, Manchester Royal Infirmary.

It appears that George Bowring could indeed have been the first person to administer general anaesthesia using ether in Manchester. John Braithwaite in his letter of 4 February, mentions: 'such trials as have yet been made at the Infirmary . . .'.

Indeed, he goes on to refer to a patient who had died little more than a week after the removal of a leg under ether anaesthesia. He also referred to two other patients who were anaesthetised in the week of 4 February. One cannot imagine that the administration of anaesthesia on 31 January by Mr Bowring, which was reported in *The Guardian* on 3 February 1847, was the first occasion on which Mr Bowring had administered general anaesthesia. It would be surprising if he had been taken to a private house to anaesthetise a lady of high respectability if he had not already had good experience with the use of ether and gained the confidence of both Dr Bardsley and Mr Turner. A note written by his son and retained in the Archives of the John Rylands Library of the Victoria University of

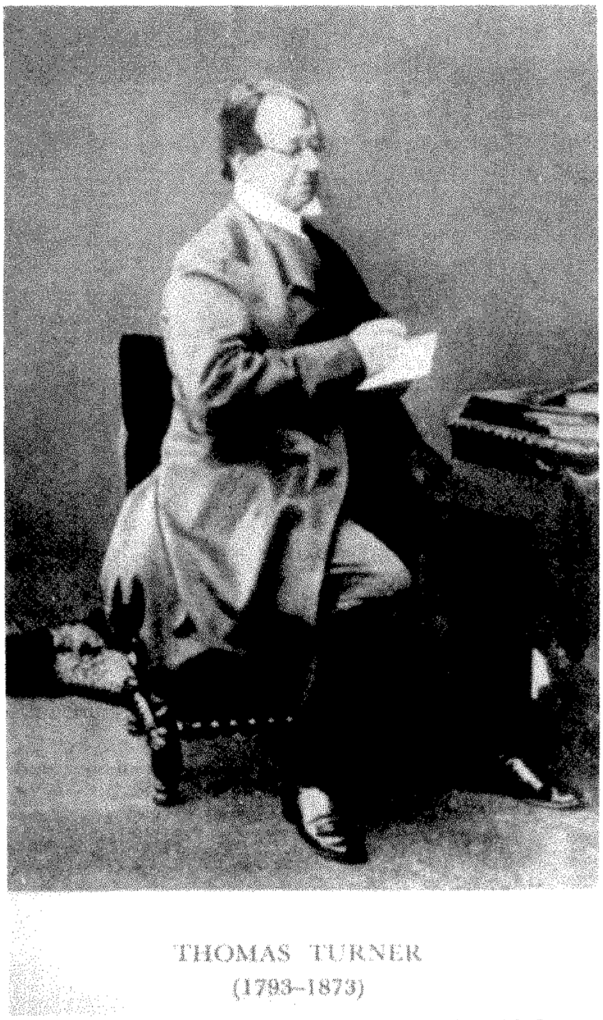

Fig. 3. Mr Thomas Turner. Surgeon, Manchester Royal Infirmary, and the Founder of the Pine Street Medical School.

Manchester records [21]: 'He told us that he administered the first anaesthetic by a doctor in Manchester.'

Certainly, both the closeness of the dates (20 days) between the letters of Charles Strange and Jas Bower Harrison and the recognition that skill was required suggest that Mr Bowring must have had appropriate experience before being permitted to anaesthetise a respectable lady in her own home. These considerations add support to the view that George Bowring administered the first ether anaesthetic in Manchester.

It is fascinating that two of the medical men mentioned in Mr Jas Bower Harrison's letter, i.e. Dr Bardsley and Mr Turner, were particularly important in the development of medical education in Manchester. Dr Bardsley (Fig. 2) was regarded as one of the leading physicians in the country and was knighted for his special services [21–25]. Mr Turner (Fig. 3) founded the Pine Street Medical School (1825) [24], the first complete School of Medicine outside London. Mr Jas Bower Harrison became an anatomy demonstrator in Chatham Street School in 1850 [24]. This school amalgamated with the Pine Street School in 1856 to form the Manchester Royal School of Medicine, which itself later combined with Owens College to establish the Victoria University of Manchester. George Bowring, a mere assistant house surgeon thus administered this anaesthetic in illustrious company.

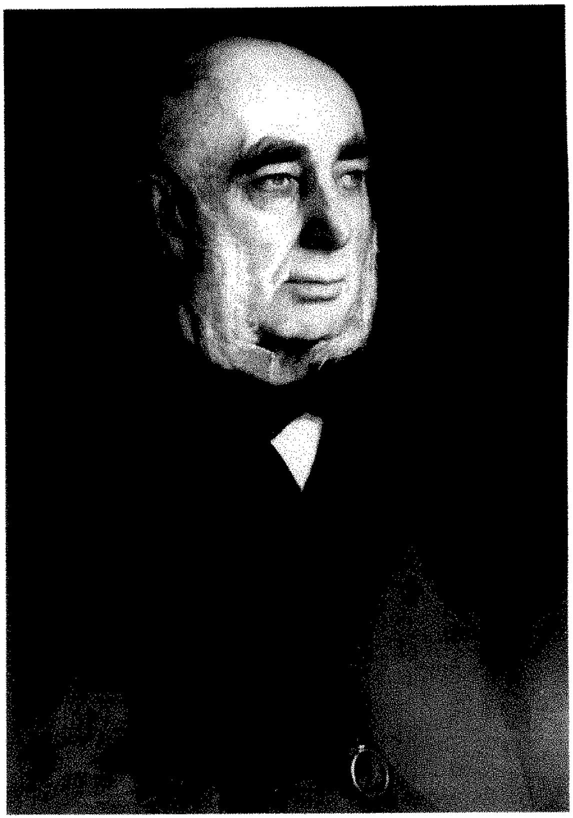

Fig. 4. Mr George Bowring. The first doctor to use ether in Manchester.

How much then is known about Mr Bowring (Fig. 4)? [26] George Bowring was born in Bradford on 17 February 1818, the son of George and Sarah Bowring of Edensor, an old family whose origins can be traced back to 1700. He studied medicine at King's College in London obtaining his MRCS in 1841 and LSA in 1843. He married Frances Walmsley of Stockport by whom he had three daughters and one son. George Bowring left King's College with glowing testimonials. We quote here from two of them [21]: 'I have known Mr George Bowring intimately from the commencement of his studies in London till the present time, he was my private pupil and hence I can bear witness to his good principles and regular habits as well as to his professional industry and talents. Mr Bowring had devoted much more than the usual time to the acquisition of practical knowledge of the various branches of his profession and he has served successfully the offices of dresser, house surgeon, clinical clerk and physician's assistant in King's College Hospital as well as that of house surgeon to the Westminster Lying-In Hospital and in all these responsible situations he ably and honestly discharged his duties so as to merit and receive the approbation and esteem of all medical officers. I beg therefore earnestly and respectfully to recommend him to the subscribers to the Manchester Royal Infirmary as a candidate for the office of apothecary to that institution. Richard Partridge, Professor of Anatomy in King's College, London and Surgeon to King's College Hospital, London, March 1st 1844.'

Other referees wrote: 'this is to certify that Mr George Bowring diligently followed the prescribed course of instruction as a matriculated student in the medical department of this College during four years, that he was regular in his attendance to the College chapel and the divinity lectures and that his conduct, as far as it came under our observation, was uniformly good. J. Litchfield, late Principal of King's College and Richard Partridge, Dean of the Medical Department and John Allen, Chaplain.'

George Bowring left London on appointment to the post of house apothecary at the Manchester Royal Infirmary, which was then situated in Piccadilly Circus, on 21 March 1844 [27]. At this time he lived at 186 Oxford Road, in a house which still stands and is situated a few hundred yards from the present Infirmary. On 19 June 1845, he was appointed Assistant Clerk to the Physicians and one year later reappointed Clerk to the Physicians. He was appointed House Surgeon on 17 June 1847, and reappointed on 22 June 1848. He was appointed to the Salford and Pendleton Royal Hospital dispensary in July 1849 [28,29]. In April 1855 he became surgeon to the Manchester Royal Infirmary and Dispensary Surgeon on 14 June 1855. The Chairman of the Board of Salford and Pendleton Royal Hospital and Dispensary wrote to Mr Bowring on 14 June 1855: 'Dear Sir, I have great pleasure in transmitting to you the following resolution past at the meeting of the Board this morning. Resolved that this Board has great pleasure bearing testimony to the abilities and kindnesses manifested by Mr Bowring in his attendance on the poor of this charity and to the great interest he has taken of the welfare of this institution since his appointment as Honorary Surgeon in July 1849. The Board of Management, Salford and Pendleton Royal Hospital and Dispensary. I remain, dear Sir, yours very truly, Mr Harvey, Chairman.'

Mr Bowring was appointed Casualty and Admitting Officer to the Manchester Workhouse and Hospital Surgeon on 7 August 1871. In due course he became senior surgeon at the Manchester Royal Infirmary. He was not reputed to be a great surgeon and was described as 'sometimes rash but extremely fast'.

It is interesting to note the attitude towards the practice of anaesthesia at that time. Byelaw Number 8 of the Manchester Royal Infirmary, as late as 1879 and 1883, still required that assistant medical officers provide anaesthesia [30]. 'No. 8. They shall on alternative days, administer chloroform when required to do so by members of the surgical staff.' New Byelaws 1883 'No. 8. They shall on Fridays and Saturdays and in special cases at other times administer chloroform when required to do so by members of the surgical staff.'

It was at a meeting of the Board in October 1886 that it was decided to advertise for a chloroformist. The Manchester Royal Infirmary Board on 29 November 1886, passed the following resolution: 5. Resolved 'That on the recommendation of the subcommittee allocated to examine applications of candidates for the appointment of administrator of anaesthetics, Alexander Wilson, MRCS, LRCP, London. He is thereby appointed to that office for 12 months from the 1st December next at £75 per annum [31].'

George Bowring lived a full and varied life and his interests spread beyond the Manchester Royal Infirmary. It is said that he had a very retiring disposition but a keen sense of humour. He was known to have a twinkle in his eye, a delightful personality and enjoyed a risqué joke. He had a bald head and wore a monocle which never seemed to drop out. He was a member of the Board of Guardians and Medical Officer to the Lancashire and Yorkshire Railway. He was Church Warden of the Manchester Catherdral during the time of its restoration and is listed in the book of Church Wardens. A small sculpted model of his head is to be seen over the archway leading into the Derby Chapel in the Cathedral (Fig. 5). He was a member of John Shaw's Club and the Manchester Literary Club and a staunch conservative. He must have been an opponent of the Corn Law because he was one of the chief guests and a speaker at a great dinner for 3800 persons on Wednesday 2 February 1844 in the Free Trade Hall in Manchester [32,33]. He died in Manchester on 3 March 1902 and his death certificate, signed by Dr A. B. Edge, MD, stated the cause of death to be senile decay [26]. At the time of his death he was living in Melbourne Cottage on Platt Lane (Fig. 6). A small block of flats now stands on this site and Sir Harry Platt lived in one of these close to the present Manchester Royal Infirmary, but in this case, the name Platt is a coincidence.

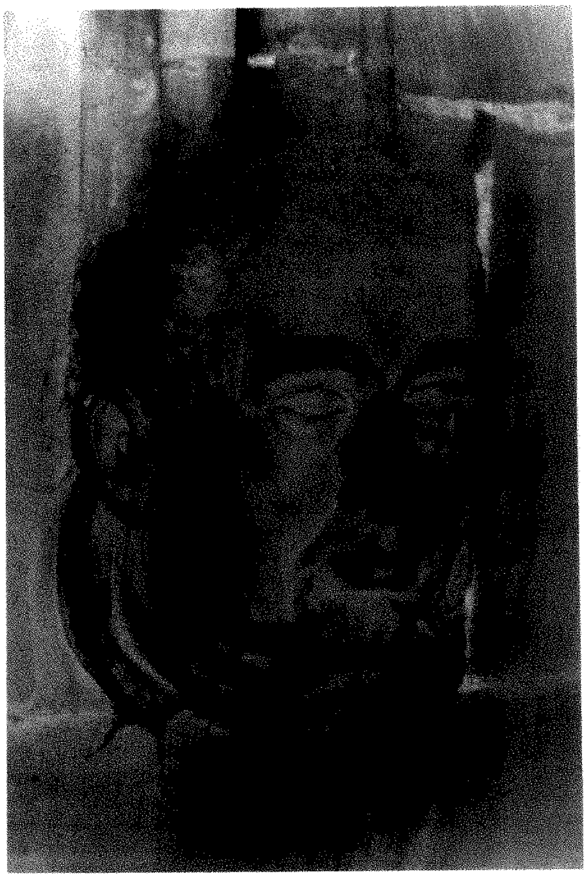

Fig. 5. Model of George Bowring's head in Manchester Cathedral.

Dentist and Surgeon, Strange and Bowring. We cannot yet be sure which of these two was the Manchester 'first'. Yet the balance of probability, taking into account the need to practise the skill thoroughly before venturing to attempt anaesthesia for a respectable woman in her own home, makes it difficult to resist the suggestion that Bowring, who claimed the first anaesthetic by a doctor in Manchester, also administered the first ether anaesthetic in Manchester. On the other hand a doubt will always persist. Strange may, if already a dentist, have previously used nitrous oxide, in which case it would have been a natural progression for him to use ether as soon as he heard of its effects. It is a mystery why the records of this momentous

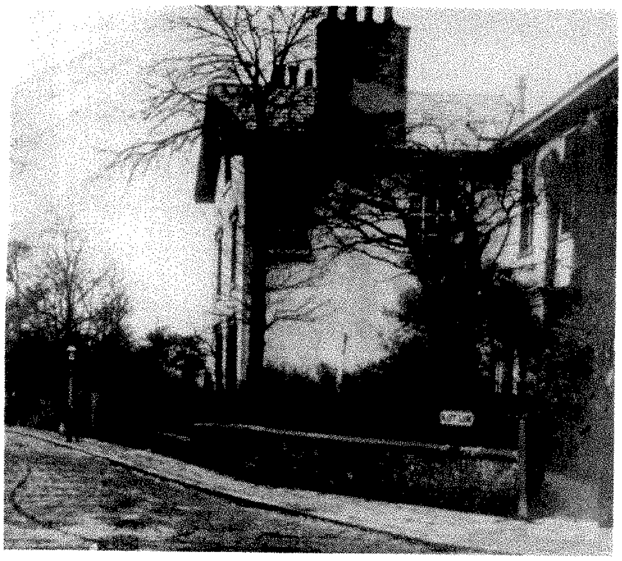

Fig. 6. Mr Bowring's home in Platt Lane.

event are so scanty. Although this chapter in our history may have had a strange opening, could Bowring with the small sculpted model of his head on the ceiling in the Cathedral, yet close it with the last word?

Acknowledgments

We acknowledge the help that we received from Dr P. Povey, District Medical Officer, Central Manchester District, Mr P. R. Helm, formerly Chairman, Rush and Fallowfield Civic Society, Mr A. Thorlby, Photographer at Withington Hospital and from the staff of the following institutions: John Ryland University Library, Manchester Central Library—Local History Section, Salford Local History Library, Greater Manchester County Record Office—County Archive Research Network, Salford Royal Hospital—Archive, The British Library Newspaper Library, The Public Record Office–Census Room, London and the Manchester Registrar (Births and Deaths).

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Anaesthesia, 1992, Volume 47, pages 887–889

Forum

Plasma concentrations of flumazenil during liver transplantation

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Summary

Six patients were given flumazenil (1 mg) during the anhepatic period of liver transplantation. We found higher mean plasma flumazenil concentrations during the anhepatic period than occurred in patients with hepatic cirrhosis. It was only possible to measure plasma flumazenil concentrations in four patients after revascularisation of the donor liver. Of these, elimination half-lives could be calculated in only three patients (normal in one and prolonged in two). In these two patients the elimination half-lives were prolonged to the same extent as in patients with fulminant hepatic failure. The changes during the anhepatic period occur because the liver contributes to the central volume of distribution. After revascularisation of the donor organ the prolonged half-lives indicate that transplanted livers may not recover normal metabolic functions immediately.

Key words

Antagonists, benzodiazepines; flumazenil.
Pharmacokinetics.
Surgery; liver transplantation.

Flumazenil has an elimination half-life of about 1 h in normal volunteers [1]. The clearance of this drug is thought to be mainly hepatic, although in common with other benzodiazepines extrahepatic metabolism [2] may occur.

In critically ill patients the dose of flumazenil needed to reverse benzodiazepine sedation is less than previously calculated [3]. This suggests that flumazenil elimination may be retarded by altered liver function, as previously described for midazolam [4].

The elimination of flumazenil in liver disease has been studied in eight patients with cirrhosis [5] and in three patients with fulminant hepatic failure [6]. We have used the anhepatic period of liver transplantation to study the elimination of flumazenil in a further six patients during a period when there is no liver function.

The operation can be divided into three periods. Firstly, the dissection period when the liver is mobilised on to its vascular pedicles. Secondly, the anhepatic period, starting when the blood vessels are clamped and the liver removed, and ending when the liver is reperfused with blood. Finally, the hepatic arterial and biliary anastomoses to the donor liver are completed, the vascular clamps removed, the liver reperfused, and the abdomen closed.

Patients and methods

Six patients undergoing liver transplantation took part in an open single dose, pharmacokinetic study of flumazenil at the start of the anhepatic period of liver transplantation. The patients gave informed consent to the study, which was approved by the Hospital Ethics Committee.

Anaesthesia and surgery were performed as described before [7], except that an opioid, usually combined with an antisialogue, was used for premedication rather than a benzodiazepine. Immediately before the start of the anhepatic period a baseline blood sample was collected. Five minutes later flumazenil (1 mg diluted to 10 ml with 0.9% saline) was given over 2 min through a central venous line and then flushed in, using a further 10 ml 0.9% saline. Blood samples were taken at 2, 5, 10, 15, 20, 30, 40 and 60 min after the injection of the drug or until the end of the anhepatic phase. This sampling protocol was repeated after revascularisation of the liver and further samples were taken at 2, 3, 5 and 9 h from the time of flumazenil administration.

The blood was separated by centrifugation and the supernatant plasma stored at $-20°C$ until analysis by gas chromatography [8]. The limit of quantification for this analytical method was 100 $pg.ml^{-1}$ and the reproducibility was 4.56 to 6.07%.

Results

Patient details including duration of the anhepatic period, urine output, blood loss and replacement are shown in Table 1. All patients produced urine during the anhepatic period indicating that the kidneys and probably other organs were well perfused. Blood loss was not excessive in any patient.

The values for the plasma concentrations of flumazenil for each patient, during the anhepatic and reperfusion period, are shown in Figure 1. It is noteworthy that the

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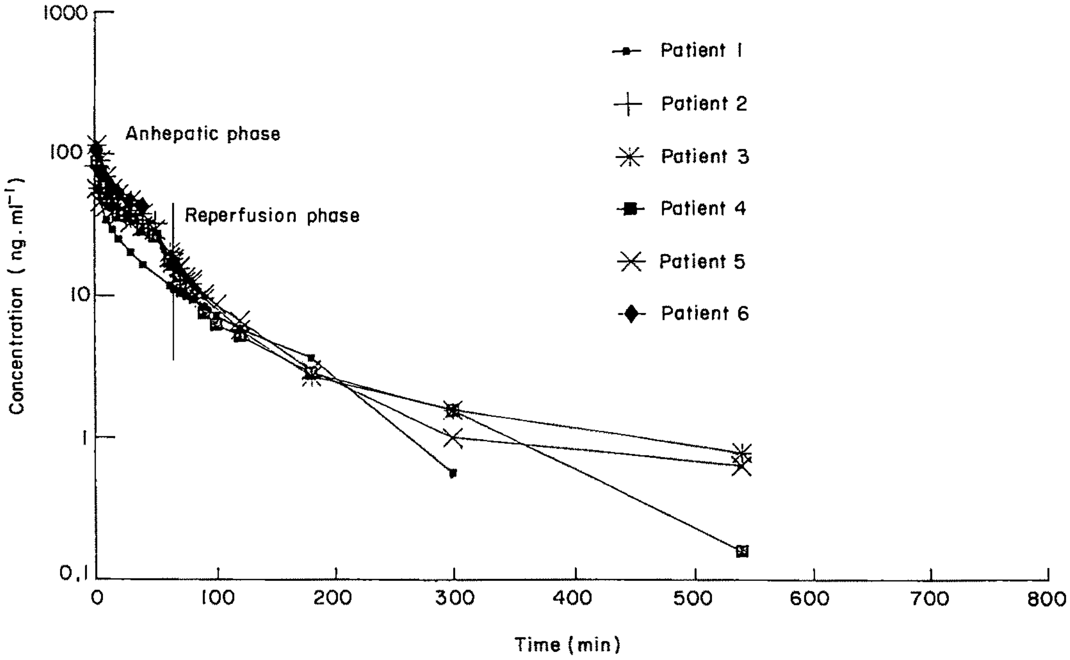

Fig. 1. Plasma concentrations after the intravenous administration of flumazenil 1 mg to six patients during liver transplantation. Values for two patients, 2 and 6, were not available.

interpatient variation is small. The mean data for all of the study are shown in Figure 2. It was only possible to measure the plasma concentrations of flumazenil after reperfusion in four patients—in the other two it was not possible to interpret the chromatograms. This fact and the need to limit the volume of blood sampled during this operation restricted the amount of data available and precluded a comprehensive pharmacokinetic analysis.

Figure 2 shows the mean plasma flumazenil concentrations in our patients compared to those found in healthy volunteers and in patients with cirrhosis [5]. The patients with cirrhosis and the volunteers both received flumazenil (2 mg), and plasma flumazenil concentrations in the figure have been dose adjusted. During the anhepatic period the flumazenil concentrations in our patients were consistently higher than those in the cirrhotic patients and healthy volunteers.

After reperfusion, plasma flumazenil concentrations decreased further and it was possible to see a linear elimination phase. We were able to calculate elimination half lives in three of the four patients in whom there were measurable concentrations of flumazenil during this period; these were 3.5 h (patient 3), 1.41 h (patient 4) and 0.93 h (patient 6).

Discussion

Previous studies, during the anhepatic period of liver transplantation, have examined the possibility of extrahepatic drug metabolism by measuring metabolites [2, 9–11]. This was not possible in this investigation as an assay for flumazenil metabolites was not available.

We have shown that the plasma concentrations of flumazenil are greater in anhepatic patients than in normal volunteers or patients with cirrhosis and have demonstrated the importance of the liver in the overall clearance of flumazenil. There is known to be an increase in plasma flumazenil concentrations in patients with cirrhosis compared to normal subjects [5] and we have shown a further four-fold increase during the anhepatic period.

It seems unlikely that the haemodynamic changes seen during the anhepatic period of liver transplantation could significantly alter the kinetics of distribution, although blood loss ranged from 200–1200 ml. It was possible to

Table 1. Patient information, duration, blood loss and its replacement along with urine output during the anhepatic period.

Patient number and sex	Diagnosis	Weight (kg)	Duration (min)	Blood loss (l)	Blood replacement (ml)	Urine output (ml)
1 F	PBC	45	45	0.3	0.2	40
2 M	AC	80	50	0.2	1	45
3 F	PBC	55	52	0.6	0.8	73
4 F	PBC	46	40	0.9	0.5	70
5 F	PBC	65	55	1.2	1.5	20
6 M	WD	57	55	0.7	0.5	30

PBC, primary biliary cirrhosis; AC, alcoholic cirrhosis; WD, Wilson's disease.

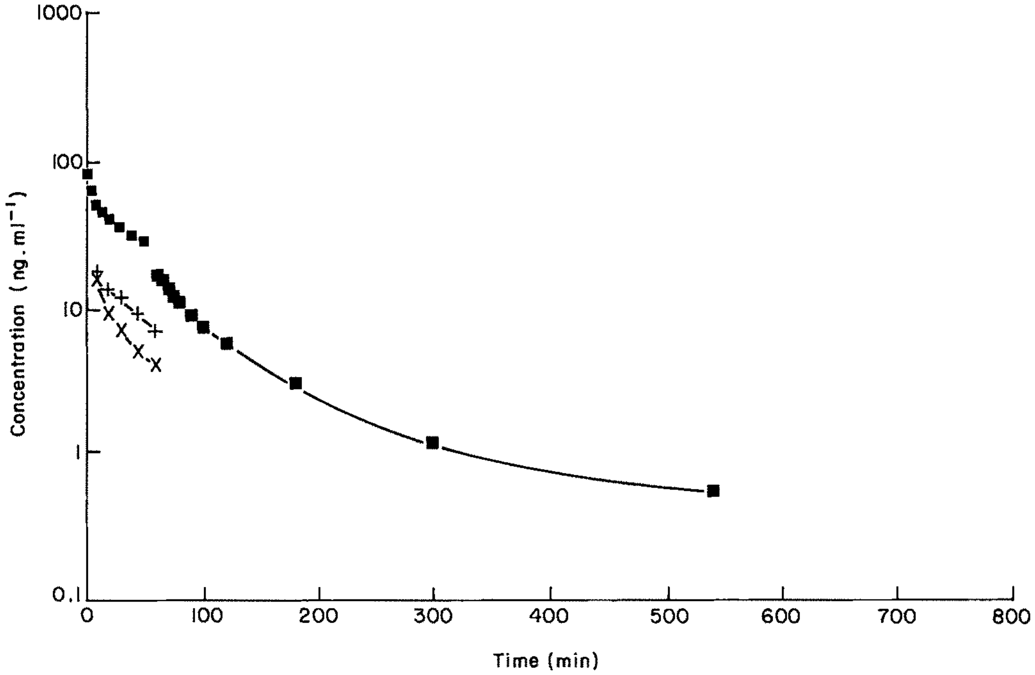

Fig. 2. Plasma concentrations after the intravenous administration of flumazenil 1 mg to six patients during the anhepatic (■) and reperfusion (■) periods of liver transplantation; eight healthy volunteers (×), and eight patients with cirrhosis (+) [5].

measure the elimination half-life, during the reperfusion period, in three of the patients. In two it was longer than in healthy volunteers [1], but similar to those reported in patients with fulminant hepatic failure [5]. This suggests that the transplanted liver recovers its metabolic activity gradually.

Acknowledgments

We gratefully acknowledge the assistance of Dr A. Bodenham, our other anaesthetic colleagues and Mr M. Smith who helped us with this study. We also thank Dr Roncari for his pharmacokinetic advice and Mr C. Husser for technical assistance with the assay.

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Anaesthesia, 1992, Volume 47, pages 890–891

Local anaesthetic: does it really reduce the pain of insertion of all sizes of venous cannula?

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Summary

A recent study performed in this department showed that a subcutaneous injection of local anaesthetic was significantly less painful than the insertion of a 22-gauge venous cannula. However, our colleagues remained sceptical that local anaesthetic infiltration would eliminate the pain of cannulation. Consequently a further study was undertaken to compare the pain of cannulation with and without the use of local anaesthetic. The results show that pain of cannulation is significantly ($p < 0.003$) reduced after subcutaneous infiltration with 1% lignocaine when compared to cannulation without local infiltration. Persistent discomfort at the site of cannulation was eliminated by the use of local anaesthetic.

Key words

Veins; cannulation.
Anaesthetics, local; lignocaine.

A survey undertaken in this department revealed that most anaesthetists did not employ infiltration of local anaesthetic before insertion of an 18, 20 or 22-gauge intravenous cannula because they believed that cannulation was less painful than injection of lignocaine. We demonstrated [1] that intravenous cannulation with a cannula of 18, 20 or 22 gauge was significantly ($p < 0.006$) more painful than a subcutaneous injection of 1% lignocaine. These results were disseminated within our anaesthetic department, but most anaesthetists remained of the opinion that the combination of local anaesthetic infiltration and insertion of an intravenous cannula (which had not been investigated) was more painful than cannulation alone.

This study was undertaken to establish whether prior injection of local anaesthetic significantly diminishes the pain of cannula insertion when using a small intravenous cannula (18–22-gauge).

Patients and Methods

The study was approved by the District Ethics Committee and written informed consent was obtained from all participants. Sixty adult patients, who were about to undergo surgery under general or regional anaesthesia, were included in the trial. Patients were allocated randomly (sealed envelope technique) into one of three groups, to receive intravenous cannulation with a Venflon cannula of 18 (group 1), 20 (group 2) or 22-gauge (Group 3). Within each group, the side of local anaesthetic infiltration was randomised equally between left and right. Patients were premedicated or not as determined by the anaesthetist.

The patient's eyes were closed throughout the procedure and a tourniquet was applied to both arms. A subcutaneous injection of 0.25 ml lignocaine 1% through a 25-gauge needle was given into the dorsum of one hand and 1 min later a Venflon of predetermined size was inserted into the vein through the site of local infiltration. A Venflon of the same size was inserted into the corresponding site in the other hand. Cannulation was performed in the left hand first in all patients.

The patients were then asked which procedure was the more painful and graded each insertion on a discrete pain scale of 1 to 10 (1: no pain; 10: worst pain imaginable). All cannulations were successful at the first attempt. After a delay of 5 min, patients were asked if either cannula site still felt uncomfortable. Data were analysed using the Wilcoxon signed rank test or Chi-squared test as appropriate.

Results

Sixty patients completed the trial: 27 were male. Mean age was 47.8 years (range 24–90).

All patients in group 1 (18-gauge) found cannulation without local anaesthetic more painful than with local anaesthetic (median pain scores 7 and 2 respectively). In group 2 (20-gauge), 16 of the 20 patients found cannulation without local anaesthetic more painful (median pain scores 5 and 2 respectively) while four patients found the infiltration more painful than cannula insertion. In group 3 (22-gauge), 15 of the 20 reported less pain following local infiltration than without (median pain scores 5 and 2 respectively); one patient thought there was no difference between the two techniques and four found infiltration more painful than cannulation. The pain score distributions of the three groups are shown in Figure 1.

The difference between pain scores for cannula insertion with and without local anaesthetic were analysed using the Wilcoxon signed rank test. This showed that venous cannulation without local anaesthetic infiltration was significantly more painful than with infiltration in all three groups (group 1, $p < 0.0001$; groups 2 and 3, $p < 0.003$).

All the sites of cannulation performed using local anaesthetic were painless 5 min after insertion, but 40 patients complained of persistent discomfort at the other cannulation site. The difference between the two methods of cannulation was statistically significant ($p < 0.0001$).

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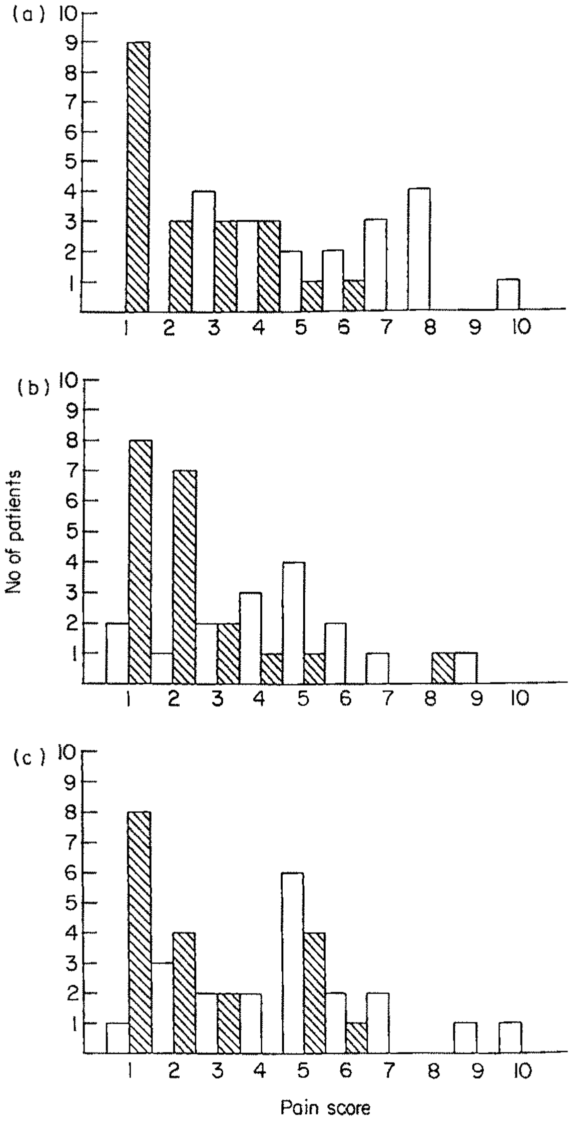

Fig. 1. Distribution of pain scores in patients in whom an intravenous cannula of 18-gauge (a), 20-gauge (b) or 22-gauge (c) was inserted into the dorsum of one hand and local infiltration followed by venous cannulation into the corresponding site in the other hand. Hatched bar; local infiltration followed by cannulation; clear bar; venous cannulation only.

Discussion

Venous cannulation is the most commonly performed invasive procedure in hospital medicine and is a source of pain and anxiety to the patient. Previous work has shown that the use of ethyl chloride spray or intradermal lignocaine [2] reduces the pain of cannulation with a 20-gauge venous cannula and it is now common practice to use EMLA cream [3] for intravenous cannulation in children.

In this department it remains unusual for anaesthetists to use local anaesthetic infiltration prior to insertion of a small (18-gauge or smaller) intravenous cannula in adults. The majority believe that the combination of local anaesthetic infiltration and insertion of a small cannula is more painful than cannulation alone. It is also argued that local anaesthetic infiltration makes cannulation more difficult. However, neither investigator found any increased difficulty associated with this method if care was taken in selecting the site for cannulation and only a small volume of local anaesthetic was used. A subcutaneous injection was used in this study, as the fluid was easier to dissipate than with an intradermal injection and therefore did not obscure the intended cannulation site.

Our study has demonstrated that local anaesthetic significantly reduces the pain of cannulation in adults without decreasing the incidence of successful cannula insertion. We have also shown that discomfort following cannula insertion is eliminated. We strongly recommend that local anaesthetic infiltration is used prior to insertion of any size of intravenous cannula. Not only does this improve patient acceptability of the procedure but it also eliminates a source of discomfort after cannulation.

Acknowledgments

We thank the nursing staff in the theatre patient reception area for their help and cooperation in this study.

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Anaesthesia, 1992, Volume 47, pages 892–895

Day case laparoscopy

A comparison of two anaesthetic techniques using the laryngeal mask during spontaneous breathing

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Summary

Forty women undergoing day case laparoscopy were randomly allocated to receive either an inhalational or total intravenous anaesthetic. All patients breathed spontaneously through a Brain laryngeal mask. There were no clinically significant cardiovascular or respiratory differences between the two techniques. No episodes of clinical aspiration occurred and there were no peri-operative arrhythmias. We conclude that spontaneous respiration with a laryngeal mask is a safe and effective method of anaesthesia for laparoscopy provided certain guidelines are followed.

Key words

Anaesthesia; day surgery, laparoscopy.
Equipment; laryngeal mask airway.

Anaesthesia for laparoscopy is a controversial subject [1, 2] and tracheal intubation has been advocated for patients undergoing laparoscopic procedures [3]. Intubation of the trachea and intermittent positive pressure ventilation ensures protection of the airway from aspiration and maintains adequate ventilation [4]. Anaesthesia without tracheal intubation may increase the risk of aspiration due to the raised intra-abdominal pressure, and ventilation may be compromised by diaphragmmatic splinting in a steep Trendelenberg position. The possibility of carbon dioxide retention in these circumstances increases the likelihood of peri-operative arrhythmias [4, 5].

Some anaesthetists have suggested that day case laparoscopy is possible with mask anaesthesia [6]. The introduction of the Brain laryngeal mask (LM) [7] offers an alternative to conventional methods of airway management during laparoscopy. This present study examined the feasibility of using the LM for anaesthesia for day case laparoscopy in spontaneously breathing patients. The efficacy and postoperative complications arising from two anaesthetic techniques were compared.

Methods

With the approval of the District Ethics Committee 40 consenting women aged 18–50 years, weighing 50–80 kg, ASA 1 or 2, and scheduled for day care laparoscopy were admitted to the study. Patients with a history of chronic lung disease or those who smoked more than 20 cigarettes daily were not studied. All patients conformed to the normal selection criteria for day surgery. They were randomly allocated to receive either nitrous oxide, oxygen, and alfentanil (group A; $n = 20$) or an intravenous infusion of propofol (Group B; $n = 20$) to maintain anaesthesia.

Both groups received a standardised anaesthetic induction technique consisting of intravenous atropine (0.3 mg), alfentanil (3 μg.kg^{-1}), propofol (2.5 mg.kg^{-1}) and papaveretum (8–10 mg). Following induction, a laryngeal mask was inserted and connected to the anaesthetic machine by a Lack breathing system. Thereafter, patients in group A breathed a mixture of nitrous oxide (66%) in oxygen supplemented by enflurane 1–4% and/or bolus doses of alfentanil (3 μg.kg^{-1}). Patients in group B (total intravenous anaesthesia—TIVA) received an infusion of propofol at a rate of 14 mg.kg^{-1}.h^{-1} for 5 min reducing to 12 mg.kg^{-1}.h^{-1} for the next 10 min and subsequently to 10 mg.kg^{-1}.h^{-1}. The infusion was controlled by an Ohmeda 9000 infusion pump. Bolus doses of propofol (0.5 mg.kg^{-1}) were given, as required, to maintain anaesthesia. A further bolus dose of alfentanil (3–5 μg.kg^{-1}) was given prior to insertion of the laparoscope. Patients in group B breathed oxygen-enriched air during the operation (4 l.min^{-1}.$_2$ and 2 l.min^{-1} air). All the anaesthetics were administered by T.W.O.

The pulse rate and systolic and diastolic blood pressures were measured noninvasively using a Critikon Dinamap. The end-tidal carbon dioxide concentration and respiratory rate were recorded by a Datex capnograph with the sampling port between the LM and the Lack breathing attachment. The inspired oxygen concentration and peripheral oxygen saturation were monitored throughout the procedure and in the immediate recovery period. A continuous peri-operative recording of the patient's electrocardiograph (ECG) was made using an ECG tracker (Reynolds Medical).

Postoperatively, patients were transferred to a recovery room in the lateral recovery position with the LM in place. Patients in both groups breathed oxygen-enriched air until they removed the airway themselves. 'Awakening' was defined as the time at which a Steward score of 6 was first

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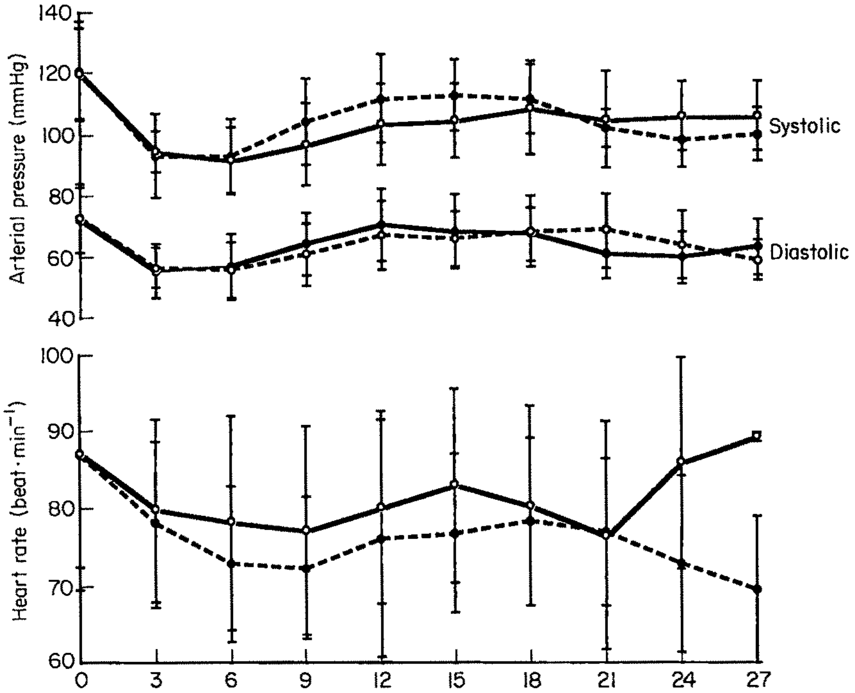

Fig. 1. Haemodynamic variables (mean, SD) throughout the peri-operative period in patients anaesthetised with a total intravenous anaesthetic technique (propolol/afentanil) or inhalational anaesthesia (enflurane/N_2O/O_2). – – –, TIVA; —, enflurane.

obtained [8]. The time from cessation of anaesthesia to 'awakening' was recorded as the immediate recovery time.

On wakening all patients were connected to a patient controlled analgesia system (Grazeby PCAS) the operation of which had been explained beforehand. This was set to deliver an intravenous bolus of alfentanil (1.5 μg.kg^{-1}) on demand with a 'lock out' time of 3 min. Patients were encouraged to use this device as required over the first 4 postoperative hours.

When a Steward score of six had been achieved patients were invited to complete 100 mm visual analogue scales for pain, nausea and headache after 30 min, 1 h, 2 h, 3 h, 4 h and 5 h.

Statistical analyses were performed using analysis of variance and Student's *t*-tests where appropriate with a p value of < 0.05 considered significant.

Table 1. Patient, anaesthetic and surgical details. Mean values (SD).

	Total intravenous anaesthesia	Enflurane
Age; years	32 (5.1)	35 (7.7)
Weight; kg	62 (8.0)	63 (7.7)
Propofol induction; mg	166.5 (14.9)	171.5 (16.3)
Propofol maintenance; mg	165 (55)	0
Papaveretum; mg	10 (0)	9.8 (0.6)
Intra-operative alfentanil; μg	466 (159)	194 (101)*
Duration of anaesthesia; min	13 (2.7)	15 (4.5)
Duration of surgery; min	10 (2.2)	12 (4.5)
Anaesthesia to awake; min	8.6 (3.9)	8.2 (3.1)
Operative procedure		
Diagnostic (*n*)	12	11
Sterilisation (*n*)	8	9

*p = 0.001.

Results

Table 1 shows the patient, anaesthetic and surgical details of both groups in the series. The overall mean operating time was 11.5 min and the volume of CO_2 insufflated never exceeded 2 l. The mean intra-operative alfentanil dosage was significantly higher in the TIVA group compared with enflurane anaesthesia (p = 0.001).

Figure 1 shows the cardiovascular values throughout the operative and recovery period. There were no significant differences between the groups in heart rate, systolic blood pressure and diastolic blood pressure.

Figure 2 shows the respiratory values throughout the operative and recovery period. There was a significant reduction in oxygen saturation in the enflurane group compared with the TIVA group at all sampling times between 3 and 24 min and a significantly higher end-tidal carbon dioxide concentration at 12 min. There were significant decreases in respiratory rate at 12 and 18 min in the enflurane group compared with those receiving TIVA.

There was no difference in postoperative alfentanil requirements between the treatment groups and there were no statistically or clinically significant differences between the groups in respect of postoperative pain, nausea or headache (Table 3).

Twenty-one patients had continuous ECG Holter monitoring throughout the 6 h peri-operative observation period

Table 2. Total mean (SD) alfentanil usage (μg) in the first 4 postoperative hours.

Anaesthetic type	Alfentanil (patient-controlled analgesia system)
Total intravenous anaesthesia	1120 (770)
Enflurane	926 (780)

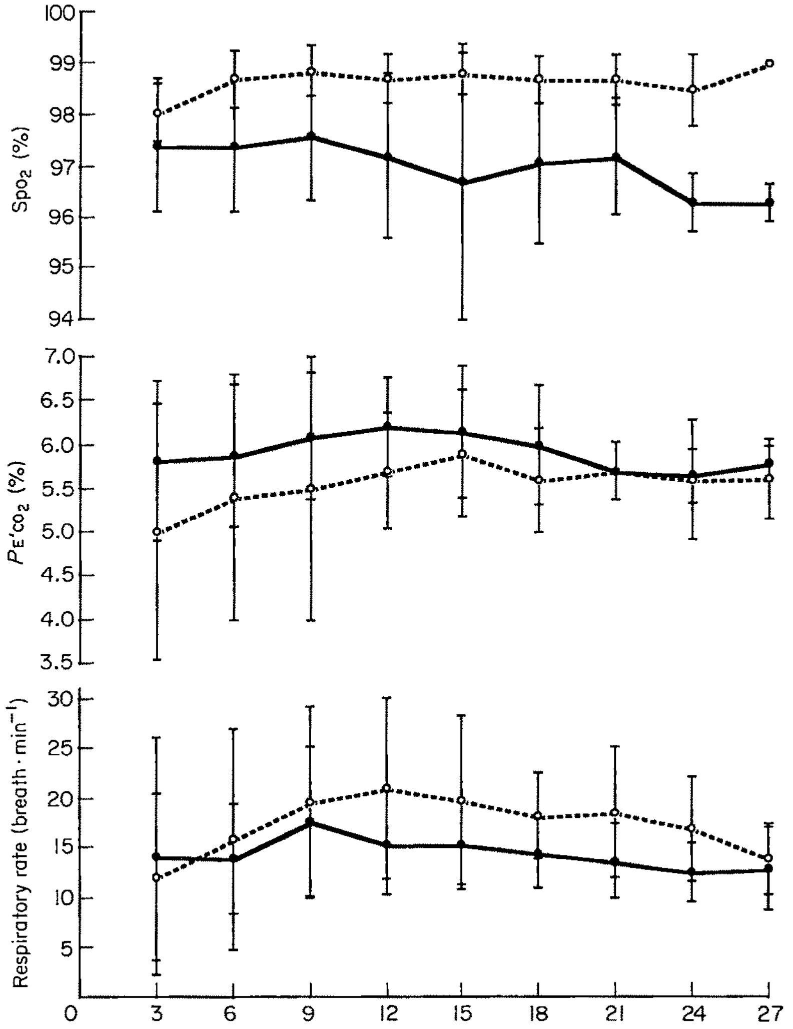

Fig. 2. Respiratory variables (mean, SD) throughout the peri-operative period in patients anaesthetised with total intravenous anaesthetic technique (propolol/alfentanil) or inhalational anaesthesia enflurane/N_2O/O_2). – – –, TIVA; —, enflurane.

and no significant arrhythmias were seen. No airway problems were encountered in either group throughout the operative period and there was no clinical evidence of peri-operative aspiration.

Discussion

Many anaesthetists are opposed to the use of spontaneous ventilation in laparoscopy [1, 3–5]. Earlier laparoscopic studies report lengthy procedures and the use of large volumes of gas to produce a pneumoperitoneum [4]. Tracheal intubation has been advocated to ensure adequate ventilation and to protect the airway from aspiration due to either raised intra-abdominal pressure or a steep Trendelenberg position. The use of the laryngeal mask in this study demonstrated that adequate ventilation was maintained in both groups of patients. However, greater ventilatory depression was demonstrated with enflurane anaesthesia compared with total intravenous anaesthesia, as shown by differences in oxygen saturation and respiratory rate.

There was no evidence of clinical aspiration during this study, a finding supported by Kurer and Welch in a study of laparoscopies lasting for 5 min with a 10 degree Trendelenberg tilt [6]. It has been suggested that longer procedures may increase the incidence of passive regurgitation [9] and we would suggest that laparoscopic procedures lasting longer than 30 min would be unsuitable for this technique.

Airway problems have been reported in 23% of patients breathing spontaneously through a face mask during laparoscopies [6] but no airway problems occurred in our study.

Tracheal intubation with either spontaneous or assisted ventilation increases morbidity following laparoscopy [6]. It has been suggested that much of this postoperative morbidity e.g. muscle pains, double vision, muscle weakness and sore throat are the direct results of the use of muscle relaxants and tracheal intubation [9–15]. As day case laparoscopies increase in number it is important that anaesthetic techniques are developed which minimise morbidity and maintain patient safety. This study suggests that anaesthesia for short laparoscopic gynaecological procedures can be safely performed using the laryngeal mask airway.

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Table 3. Visual analogue scores (mm; median and range) for pain, nausea and headache throughout the postoperative period after achieving a Steward score of 6.

Time	TIVA		Enflurane	
(min)	Median	(range)	Median	(range)
Pain				
30	33.0	(2–70)	16.0	(0–100)
60	22.0	(0–58)	19.0	(0–55)
120	13.0	(0–44)	7.0	(0–33)
180	8.5	(0–25)	6.0	(0–18)
240	5.0	(0–25)	4.5	(0–31)
300	4.5	(0–19)	6.0	(0–32)
360	8.0	(0–20)	5.5	(0–52)
Nausea				
30	0.5	(0–30)	0	(0–16)
60	0.5	(0–6)	0	(0–8)
120	0	(0–22)	0	(0–17)
180	0	(0–77)	0	(0–8)
240	0	(0–71)	0	(0–28)
300	0	(0–58)	0	(0–8)
360	0	(0–58)	0	(0–73)
Headache				
30	0.5	(0–12)	0	(0–17)
60	0	(0–7)	0	(0–6)
120	0	(0–3)	0	(0–10)
180	0	(0–23)	0	(0–10)
240	0	(0–18)	0	(0–29)
300	0	(0–16)	0	(0–22)
360	0	(0–64)	0	(0–24)

TIVA = Total intravenous anaesthesia.

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An audit of induction of anaesthesia in neonates and small infants using pulse oximetry

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Summary

The frequency and severity of hypoxaemia during induction of anaesthesia in neonates and small infants at the Norfolk and Norwich Hospital, a district general hospital, was compared, using pulse oximetry, with that of the nearest specialist hospital, the Queen Elizabeth Hospital for Sick Children in London. There were differences in staffing and the choice of anaesthetic techniques between the hospitals. One third of the patients in both hospitals experienced desaturation of more than 5% (moderate or severe hypoxaemia) at one or more recordings during induction. The highest incidence of hypoxaemia was associated with awake intubation. There was no statistical difference in the incidence or severity of hypoxaemia between the hospitals. In the district general hospital, moderate or severe hypoxaemia of greater than 30 s duration was more likely if an anaesthetist with a regular paediatric operating list was not present at induction ($p < 0.01$).

Key words

Anaesthesia; paediatric, audit.
Monitoring; pulse oximetry.

Anaesthesia for neonates and small infants is an area of district general hospital practice where high standards are difficult to achieve. A variety of administrative problems need to be overcome to ensure optimum use of the small number of opportunities to maintain or enhance the necessary skills [1]. There was therefore a need to appraise the level of expertise in the field offered by existing staff in Norwich where there is no specialist paediatric anaesthetist but a paediatric surgeon has recently been appointed.

The skill of the anaesthetist is likely to influence the incidence of hypoxaemia at induction [2]. Our object was to use pulse oximetry to compare the frequency and severity of hypoxaemia during induction of anaesthesia in neonates and small infants in Norwich with that of The Queen Elizabeth Hospital for Sick Children in Hackney, London (QEH), the nearest specialist hospital. QEH is staffed by consultant paediatric anaesthetists and post-fellowship trainees from The Hospital for Sick Children, Great Ormond Street, London, but was expected to have a case mix comparable to the Norfolk and Norwich Hospital in Norwich (N&N).

Methods

Patients. For a period of 6 months all infants who weighed less than 5 kg, who needed tracheal anaesthesia for surgery and who were breathing air without any form of ventilatory support on the day of operation were studied at the N&N. Patients who met the same criteria at the QEH were studied subsequently to provide a group approximately the same size.

Anaesthetists. In every case the anaesthetic was given by the appropriate duty anaesthetist and no constraints were imposed as to the choice of anaesthetic technique.

Equipment. A Physio Control Lifestat 1600 pulse oximeter with a recorder (pattern number 804-835-00) was used to digitally display oxygen saturation, heart rate and signal strength at intervals of 15 s. The data and real time were recorded automatically. There was a space on the chart for patient identification.

Procedure. The pulse oximeter probe was attached while the infant breathed air for at least 1 min before the anaesthetist indicated a starting time on the recorder chart. The recorder was allowed to run continuously until 1 min after the anaesthetist was satisfied with intravenous access and tracheal intubation. If a satisfactory recording could not be obtained this was noted. Throughout induction the anaesthetist was aware of the oxygen saturation. The anaesthetist was asked to complete a study record sheet indicating the anaesthetic technique used and the name(s) of the anaesthetist(s) and the operating theatre technician. Note was taken from the patient's records of the gestation at birth, age, weight, haemoglobin concentration, the nature of the proposed surgery and any concurrent medical conditions. When the study was concluded, the oximetry recordings were inspected by authors from both hospitals.

Definition of hypoxaemia and quality of recording. Hypoxaemia was defined as a pulse oximetry reading which was less than the lowest level recorded while the infant was breathing air before induction of anaesthesia. The hypoxaemia was called 'moderate' if the level fell to a saturation 6% to 10% lower than the pre-induction level and 'severe' if more than 10% lower. The quality of the oximetry recording was considered 'good' if an unequivocal trace was obtained, and 'adequate' if in the interpretation of the result allowance was made for short periods of probe disconnections and poor pick-up during the recording. Finally, if interpretation was not possible, recordings were

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Table 1. Patient data: values expressed as median (range).

	N&N ($n = 29$)	QEH ($n = 30$)
Gestation at birth; weeks	39 (26–42)	36 (25–41)
Age; days	27 (1–124)	40 (1–388)
Weight; kg	3.5 (2.0–4.9)	3.7 (1.1–4.9)
Haemoglobin; $g.dl^{-1}$	15.2 (9.0–18.5)	11.3 (8.9–20.1)
Pre-induction saturation; %	97 (91–100)	97 (90–100)

classified as 'poor' and rejected. It was anticipated that the two groups might not be the same size because it was not possible to predict that the proportion of rejected recordings would be equal.

The number of 15 s recordings of hypoxaemia, and the highest number of consecutive recordings, at the defined levels of severity, were entered on the data base.

Statistical analysis. The statistical significance of any differences were analysed using the Fisher's exact and the Mann–Whitney *U* tests as appropriate and $p < 0.05$ was considered significant.

Results

Patients. Out of a total of 36 consecutive babies, who fulfilled the inclusion criteria for audit in the N&N over the study period, oximetry recordings were not obtained for four of them. Two babies with gross upper airway abnormalities were not studied, one with Goldenhar syndrome with a pre-induction saturation of 68% and with Trisomy-18. One recording was poor and was rejected. There were 24 good and five adequate recordings.

At the QEH, 38 similar babies were anaesthetised during a 15-week period. Oximetry recordings were not obtained in three patients. Five recordings were poor and were rejected, there were 23 good and seven adequate recordings in this group.

Differences between the two hospitals in the maturity of the patients at birth and their age on the day of surgery were not significant. The weights of the patients in the two groups were similar. The median pre-operative haemoglobin concentration of the QEH patients was lower, but the difference between the hospitals was not statistically significant. The median pre-induction oxygen saturations were identical (Table 1).

Surgical diagnoses. Inguinal hernia, pyloric stenosis and small bowel atresia were the most common indications for surgery in both hospitals (Table 2). There were differences between the two hospitals with regard to the anaesthetic management of repair of cleft lip. The two infants with cleft lip in the QEH group were anaesthetised for removal of sutures. Three infants in the N&N group were anaesthetised for repair of cleft lip and although they returned to the operating theatre within the study period for removal of sutures under anaesthesia, their tracheas were not intubated for the second anaesthetic and therefore did not meet the inclusion criteria for audit. Three patients at the N&N, listed in Table 2 as miscellaneous, had meconium ileus, facial naevus and intracranial haemorrhage for CT scanning. At the QEH, the four miscellaneous patients were anaesthetised for perforated necrotising enterocolitis, colostomy for Hirschsprung's disease, burst abdomen and oesophagoscopy following repair of tracheo-oesophageal fistula.

Two patients in the N&N group and one patient in the QEH group had congenital heart disease concurrent to their surgical conditions.

Hypoxaemia at induction. A pulse oximetry reading more than 5% lower than the pre-induction level was recorded for nine of the 29 patients at the N&N and 10 of the 30 patients at QEH. A fall of more than 10% (severe hypoxaemia) was experienced by seven patients in each hospital (Table 3).

Two patients in each hospital had more than two consecutive 15 s recordings of severe hypoxaemia. Two patients at the N&N and three patients at QEH had one or two 15 s recordings of moderate hypoxaemia without more severe episodes. Three patients at the N&N and one at QEH experienced severe hypoxaemia without a period of moderate hypoxaemia.

Choice of induction techniques. There were differences between the hospitals with regard to the choice of induction techniques. Over 75% of babies in the QEH group received inhalational induction and the remainder were given intravenous induction. By contrast, only 35% in the N&N group were induced by inhalation and 41% via the intravenous route (Table 4). When data from both hospitals were pooled in order to compare induction techniques, inhalational induction had the lowest incidence of hypoxaemia followed by intravenous induction (Table 5). This difference was not statistically significant. Attempts at awake intubation were associated with the highest incidence of hypoxaemia.

Anaesthetists. Consultant anaesthetists were present in 26 of the 29 cases at the N&N and in 24 of the 30 QEH cases. However, whereas in the N&N the anaesthetic was administered in 24 cases by a consultant, at QEH, on half of the occasions when a consultant was present, it was in a supervisory role.

In Norwich, 23 patients were anaesthetised by consultants with regular paediatric operating lists. Six patients

Table 2. Surgical diagnoses.

	N&N ($n = 29$)	QEH ($n = 30$)
Pyloric stenosis	10	5
Inguinal hernia	7	12
Small bowel atresia	3	4
Cleft lip	3	2
Ano-rectal pathology	2	2
Gastroschisis	1	1
Miscellaneous	3	4

Table 3. Number of patients hypoxic during induction.

Number of 15 s recordings of hypoxaemia	N&N ($n = 29$)		QEH ($n = 30$)	
	Moderate	Severe	Moderate	Severe
1–2	6	4	9	4
3–4	0	2	0	2
5–6	0	1	0	1

Table 4. Type of induction.

	N&N ($n = 29$)	QEH ($n = 30$)
Inhalation	10	23
Intravenous	12	7
Awake intubation	5	0
Anaesthetised after failed awake	2	0

Table 5. Hypoxaemia related to induction (both hospitals).

Type of induction	No of patients	Number (%) with moderate or severe hypoxaemia
Inhalation	33	9 (27%)
Intravenous	19	6 (32%)
Awake intubation	7	4 (57%)

were anaesthetised by consultants without a regular paediatric operating list or by senior registrars without a consultant present. Moderate or severe hypoxaemia for more than two 15 s recordings did not occur when a consultant with a regular paediatric operating list was present, but occurred on three of the six occasions when one was absent. This difference is statistically significant ($p < 0.01$).

Operating theatre technicians. Although in Norwich the level of skilled assistance for anaesthesia was more variable than at the QEH, the vast majority of infant anaesthetics were performed with the help of one of the two operating department assistants with the most paediatric experience.

Time of surgery. In both hospitals three quarters of babies were operated upon during daylight hours between Monday and Friday.

Discussion

The surgical diagnoses and patient characteristics were remarkably comparable between the two hospitals. The median values for gestation and pre-operative haemoglobin concentrations were lower and the median value for age on the day of operation was greater in the QEH group of patients. However, these differences were not statistically significant when examined by tests which may legitimately be applied to samples of this size and distribution. A fall in arterial partial pressure of oxygen would be associated with a greater fall in arterial oxygen saturation if the oxygen haemoglobin dissociation curve were shifted to the right in an anaemic patient. To avoid desaturation during induction of anaesthesia in an anaemic patient would then be a more stringent test of skill.

In both hospitals, difficulty was experienced in obtaining pre-induction pulse oximeter recordings, which were free from movement artifact. This difficulty accounted for most of the recordings which were abandoned at the time or rejected later. It would be ideal to put the pulse oximetry probe on the right hand, which is perfused by pre-ductal blood, but although this was attempted, the site of the intravenous cannula or the patient's movement commonly made this impossible.

The definitions of moderate and severe hypoxaemia were designed to take account of differences in pre-induction oxygen saturation between patients. There is little doubt that, although no overt attempt was made to influence usual practice, the pulse oximetry display demanded by the protocol reduced the incidence of hypoxaemia. In a single blind study of pulse oximetry in two groups of 76 anaesthetised children by Coté and colleagues [3] the frequency of major hypoxic events (oxygen saturation $\leq 85\%$ for ≥ 30 s) was twice as great in the group in which the pulse oximeter was not available to the anaesthetist.

It cannot be assumed that a recording made after an interval of 15 s represents the pulse oximetry reading for the entire preceeding 15 s period. However, it is reasonable to assume that three consecutive hypoxaemic recordings represent more than 30 s continuous hypoxaemia. On this basis at least 7% of the infants studied in both hospitals suffered a fall in oxygen saturation of more than 10% for more than 30 s. One third of subjects in both hospitals experienced a fall in saturation of at least 5%.

In both hospitals a consultant anaesthetist was present in the anaesthetic room for nearly all of the anaesthetics. However, in Norwich the majority of the anaesthetics were administered by consultants. Thus, District General Hospital consultant anaesthetists need to take the infrequent opportunities offered to them to anaesthetise small babies to maintain their skills. At QEH, on the other hand, the consultants were commonly present in a supervisory role as would be expected in a postgraduate teaching hospital.

One of the incidental findings of this study is the move away from awake intubation by anaesthetists with a regular paediatric practice. This has been brought about by a number of factors. Foremost amongst these is the desire to avoid inflicting unpleasant experiences on newborns unless absolutely necessary. Also there is concern about periventricular haemorrhage resulting from fluctuations in arterial and intracranial pressures [4]. Although these have not been substantiated [5, 6], there is, as we have found, a considerable incidence of hypoxaemia assocated with this procedure. It may, however, be possible to attenuate this by using an oxygen delivering laryngoscope for intubation [7]. The successful awake intubations in our series occurred in infants in the first 3 days of life; thus, the incidence of hypoxaemia may be reduced by confining awake intubation to the newly born unless there is a strong indication (such as an upper airway abnormality or the infant is moribund).

In Norwich, there is no formal paediatric on-call rota among the consultant anaesthetists and the duty consultant for the day was usually responsible for any infant requiring general anaesthesia. Nevertheless, most procedures in this age group were undertaken during daylight hours and anaesthetists with regular paediatric operating lists were usually approached to oversee such cases.

Despite differences in staffing and choice of technique the frequency and severity of hypoxaemia during induction was remarkably similar. In both hospitals the median pre-induction oxygen saturation was 97% and fell by more than 5% for at least one recording in one third of the patients.

Lackcock and McNicol [8] found that about 40% of the children who were aged less than one year suffered a maxiumum fall to less than 90% saturation during induction of anaesthesia. During general anaesthesia, 54% of newborn and 26% of infants suffered a fall in saturation to 85% or less for at least 30 s in a group of 13 newborns and 27 infants reported by Schulz and colleagues [9]. These episodes were almost evenly distributed between induction and awakening from anaesthesia and only one episode occurred during maintenance.

We have confirmed that pulse oximetry during induction is a useful way of auditing anaesthetic practice and have provided some evidence that in a district general hospital small babies should be anaesthetised by consultants with regular paediatric work. We found no evidence to suggest that babies under 5 kg would be at less risk from hypoxaemia during induction of anaesthesia if they were transferred from the Norfolk and Norwich to the nearest paediatric hospital. However, it should be emphasised that when the majority of small babies are anaesthetised in this district general hospital there is a consultant with regular paediatric work present.

Acknowledgment

We are extremely grateful for the whole hearted support of our colleagues in performing this audit.

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Patient controlled analgesia—assessment of machine feedback to patients

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Summary

The effect of varying patient-controlled analgesia machine feedback was studied in two groups of patients following a standard surgical procedure using patient controlled analgesia with morphine to control postoperative pain. Analgesic demands, morphine consumption, pain scores and side effects were compared and comments from the patients were noted. There was no significant difference between those whose machines signalled only successful demands compared with those who had every demand acknowledged. The patients in the former group appreciated the extra input and the nursing staff found this machine configuration to be less disturbing to the ward. There was no evidence of a clinically useful placebo effect in the latter group.

Key words

Pain; postoperative.
Analgesia; patient-controlled, feedback.

Patient-controlled analgesia (PCA) has become an established method of controlling postoperative pain. Part of the benefit has been attributed to the sense of control which patients have over their treatment and improved comfort [1]. In order to allow each bolus dose to have its effect, a lockout interval is necessary; demands made within this interval are unsuccessful. The patient may or may not be aware of these unsuccessful demands depending on whether auditory or visual feedback is available from the machine. Various methods of feedback have been used ranging from a pilot light and bleep (Graseby PCAS) [2], to a sophisticated speech synthesiser [3].

The Abbott Life Care PCA Plus Infusor 4200 (Abbott Laboratories Ltd, Maidenhead, Berkshire, SL6 8JG, UK) can be programmed to bleep either when a successful demand is received or, alternatively, each time a demand is made. White refers to the latter configuration as giving a 'placebo effect' [4]; however, there is no evidence confirming any advantages of either mode of operation. This study was designed to compare the two modes.

The hypothesis tested was based on the assumption that a placebo effect exists in patients receiving a bleep with each request, which results in less analgesic use with similar or lower pain scores. Using data (variance) from similar patient groups, we calculated that 40 patients were required to detect a 30% difference in morphine consumption with p value of 0.05 and power of 0.8 [5]. A 30% reduction in morphine dose with equivalent pain relief may be associated with less opioid side effects and therefore would be clinically useful.

Methods

Permission for the study was granted from the hospital ethics committee. Forty ASA1 patients scheduled for total abdominal hysterectomy with or without bilateral salpingo-oophorectomy were studied. The patients were not taking any other form of analgesia and had normal hearing. Informed, written consent was obtained and a full explanation of PCA was given. To avoid bias, the exact nature of

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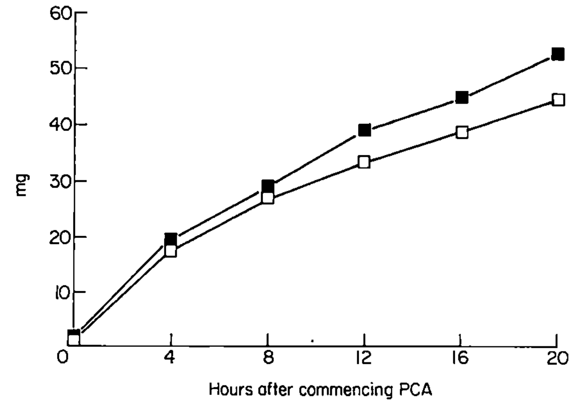

Fig. 1. Cumulative morphine consumption. ■, A; □, B.

the study was not discussed with the patients and they were only told that some aspects of the machine set-up were being examined.

Patients received temazepam 30 mg by mouth 1 h before induction of anaesthesia with fentanyl 5 μg.kg^{-1}, thiopentone 3–5 mg.kg^{-1}, atracurium 0.5 mg.kg^{-1} and enflurane 0–1% in 70% nitrous oxide. All operations were performed by one surgical team after which the neuromuscular blockade was reversed and the patients taken to the recovery room. Fentanyl was used as the intra-operative analgesic since this was the preference of the anaesthetists involved. The dose used had been found to allow patients to recover pain free without high supplementary bolus doses.

Patients were randomly allocated to receive PCA using an Abbott Life Care PCA Plus Infuser either in mode A—programmed to bleep only with successful demands, or in mode B—bleeping with every request. Both machines had screening around the control panel allowing the displays to be seen by staff and not by the patients. The infusers contained morphine sulphate solution 2 mg.ml^{-1} and were connected to the patients' intravenous infusions by means of nonreturn valves. The machines were set to deliver a bolus dose of 1 mg with a lockout interval of 5 min, no 4 h limit was set. Prochlorperazine 12.5 mg 4 hourly as required was prescribed for nausea but no other sedative or analgesic drug was allowed.

On waking, the patients were reminded of the PCA device and a further explanation of their particular machine operating in either A or B mode was given. Loading doses, where necessary, were administered by the anaesthetist and the patients were returned to the ward when confident about using their machines. Routine post-operative observations, together with assessment of sedation, respiratory rate and resting pain score were recorded hourly for 4 h and then 4 hourly as part of the normal ward observations. The pain score used was a verbal report scale (VRS) made by the patient on the scale 0—10 (where 0 represents no pain and 10 the worst pain imaginable) and this was recorded by the ward nurse. A value of 0 was recorded if the patient was sleeping at the time of observation.

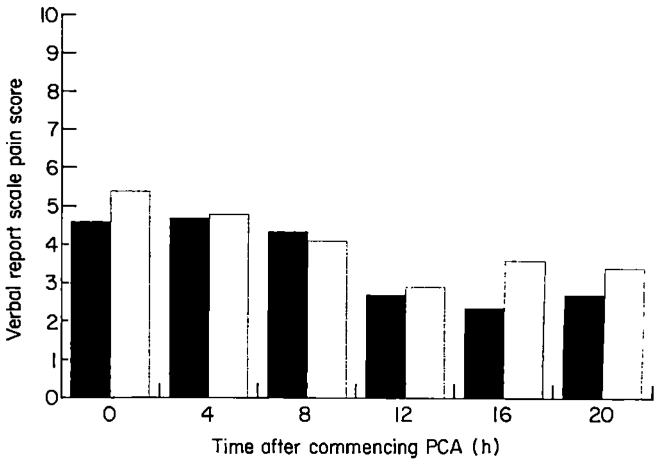

Fig. 2. Resting pain scores. ■, A; □, B.

The 4 hourly data for pain and total morphine consumption were recorded on the study sheet by the nurse observers during the study. A printout of demand history was made from the infuser after 20 h when the study was concluded. Also at this time pain scores at rest and on movement (VRS 0–10) and the number of episodes of vomiting were recorded by the anaesthetist. Antiemetic use was recorded from the prescription sheet. Comments from each patient were sought and also from the nursing staff during and at the completion of the study.

Statistical significance for the differences in the unpaired data for morphine consumption, number of demands, doses of antiemetic and episodes of vomiting were calculated using the two sample *t*-test for parametric data. Median pain scores were similarly compared using the Wilcoxon Rank Sum test for nonparametric data [6].

Results

Operations were performed between 0900 and 1100 h. All patients were able to complete the study and there were no serious complications. Patient details appear in Table 1. There are no differences between the two groups with respect to operation, age or weight.

Figure 1 shows the average cumulative doses of morphine during the study.

The differences between the groups at 20 h are shown in Table 2 and measures of variance and probability are included. The mean consumption of morphine includes the loading doses given to three patients (two from group A received 3 mg and 5 mg, one from group B received 6 mg). Patients in group A used more morphine than group B but this difference was not statistically significant at 20 h or at any other time during the study. Neither was there any significant difference in the average number of demands made by the patients.

Figure 2 shows the median resting pain scores which are similar in the two groups. Comparison at 20 h (Table 2) demonstrates no significant difference. The maximum difference in pain scores was at 16 h, but again the differ-

Table 1. Patient details.

Machine	A	B
Hysterectomy only	18	17
Hysterectomy and salpingo-oophorectomy	2	3
Mean age; years (SD)	44 (7.0)	45 (9.7)
Mean weight; kg (SD)	67 (9.2)	64 (6.1)

Table 2. Differences between groups at 20 h.

Machine	A	B	p value
Mean total morphine; mg (SD)	52 (19.8)	44 (17.5)	0.2
Mean total demands; (SD)	119 (86.7)	88 (57.5)	0.2
Median pain score			
Rest	3 (4)	4 (3)	0.25
Movement	7 (4)	8 (2)	0.5

ence was not significant. There were no differences between the groups with respect to episodes of vomiting, or antiemetic dosage.

Comments from the patients were generally favourable, although for many it was their first experience of surgery and they were unable to compare this analgesia with other methods. Two patients from group B volunteered that they found it difficult to tell whether the machine was delivering morphine. A further two agreed that this was a problem when specifically asked about the bleeping. When questioned about the bleeping, 10 (50%) of the patients in group A thought that their machine was helpful in its feedback, increasing confidence that the machine was working correctly and that analgesia was being delivered safely. Eight patients from group A and three from group B thought that at some time they were unable to obtain enough analgesia.

The nursing staff did not notice any difference between the analgesia provided by either mode of operation although some commented on the disturbance caused to other patients on the ward by the frequent bleeping of some of the group B patients' machines.

Discussion

The two groups experience different feedback. When operating in mode B, a bleep with each request results in more auditory signals reaching the patient; however, this gives less information than the machine in mode A which only bleeps when morphine is actually delivered. The results indicate that the possibility of a significant clinical benefit from a placebo effect in group B can be dismissed.

Differences between the groups may occur for other reasons. In group A the patients are aware that some demands are unsuccessful and they are likely to continue to request analgesia until success is achieved. This explanation is compatible with the observed trend towards more requests in group A. Increased knowledge of the lockout period may enable the rate of self-administration to be maximised as has been reported with use of the Graseby PCA machine [2]. Patients with this advantage would be expected to use slightly more morphine again in keeping with the trends in the study.

The variation in demand rate was wide; patients making infrequent demands are unlikely to be affected by differences in feedback as most of their demands will be successful. The differences might be greater if those with low pain thresholds or those undergoing more painful procedures (e.g. upper abdominal incisions) were studied. This study was designed to detect a difference in morphine consumption of 30% and the results do not exclude smaller differences between the groups.

Patient comments suggest a preference for mode A, although more in this group thought that at some time the analgesia was inadequate. This may have been caused by frustration at the increased awareness of the lockout interval provided by the extra feedback but was not reflected in higher pain scores. Owen and colleagues have previously noted that patients prefer more feedback [7] and our findings support that observation.

In conclusion, patients and nurses prefer greater auditory feedback during PCA although there is no obvious clinical benefit in respect of morphine use, side effects or pain scores. There may, however, be smaller differences between the groups not detected by this study. Feedback may modify analgesic demands and should be carefully controlled in studies using PCA.

Acknowledgments

The authors are grateful for help from the staff of Wheal Agar ward and the theatres at Redruth Hospital. Abbott Laboratories kindly loaned the PCA apparatus used for the study.

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Anaesthesia, 1992, Volume 47, pages 902–903

Spinal anaesthesia for urological surgery

A survey of failure rate, postdural puncture headache and patient satisfaction

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Summary

A survey was conducted on 100 consecutive patients who underwent spinal anaesthesia in our urology operating theatres. Details of the spinal technique were recorded in the operating theatre. In 25% of patients, more than one attempt at subarachnoid puncture was required and 16% of this group went on to require general anaesthesia. The patients were visited between 24 and 48 h postoperatively by one of the authors. On questioning, 24% of patients reported a headache, which had the characteristics associated with dural puncture; 62% of these headaches were described as moderate or severe and lasted between 12 and 24 h. Patients were significantly ($p < 0.05$) more likely to develop a postdural puncture headache if more than one attempt at subarachoid puncture was made.

Key words

Anaesthetic techniques regional; spinal.
Complications; headache.

It is common practice among anaesthetists to use spinal anaesthesia for some urological procedures, particularly transurethral resection of prostate (TURP) or of tumour (TURT). In obstetric practice, there has been a great deal of interest in the occurrence of headaches after spinal anaesthesia, and in methods of minimising their incidence. There has been much less interest in examining these problems in the urological patient. A previous study [1] reported a 4% incidence of postdural puncture headache in patients aged over 60 years.

The majority of anaesthetists in our department believe that postdural puncture headache in this age group is rare if a 26-gauge Yale spinal needle is used. However, there is no firm evidence to support this belief. We therefore carried out an audit of urological spinal anaesthetics in an attempt to provide further information on this topic.

Methods

Details of 100 consecutive patients who underwent spinal anaesthesia for urological procedures were recorded by the anaesthetist in the operating theatre. The following information was obtained for each patient: age; gauge and type of spinal needle; number of attempts at dural puncture; success or failure of the technique. No attempt was made to standardise the technique used to perform the spinal anaesthetic, or the subsequent management. All the patients were visited between 24 and 48 h postoperatively by one of the authors. Specific enquiry was made regarding the occurrence and duration of a postoperative headache which was characteristic of dural puncture, i.e. a postural headache aggravated by standing, relieved by lying down and fronto-occipital in distribution. Severity of the headache was assessed as described in a recent report [2]: slight, patient able to walk and requiring occasional analgesics; moderate, preventing activity and requiring analgesic therapy; severe, preventing the patient from getting up, and associated with nausea and photophobia.

Patients were also asked about their overall satisfaction with the anaesthetic technique used.

Results

All of the 100 patients were visited postoperatively. A total of 98 were male and the age range was from 50–88 years (mean 71 years). A 26-gauge Yale needle was used on 97 occasions; in four of these patients, a 22-gauge needle was used after initial failure. In three patients, a 22-gauge needle was used as the first choice.

Dural puncture was successful at the first attempt in 75% of patients and at the second attempt in 13%. In one patient, eight attempts were made at dural puncture before the technique was abandoned and a general anaesthetic was performed. Failure to locate the subarachnoid space occurred in 4% of patients, all of whom went on to receive a general anaesthetic.

In total, 24% of patients complained of a headache which was postdural puncture in nature; 62% were described as moderate or severe and lasted 12–24 h (Table 1). All of the patients responded to bed rest and simple analgesics for their headache. Of the 24 patients with a postdural puncture headache, 14 had required one attempt at locating the subarachnoid space; the remaining 10 required two or more attempts. Patients were significantly ($p < 0.05$; Chi-squared test) more likely to develop a headache if more than one attempt had been made to locate the subarachnoid space. The gauge of needle appeared not to influence the incidence of headache;

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Table 1. Number of attempts at dural puncture related to severity of postdural puncture headache.

No. of attempts	Headache severity			
	None	Slight	Moderate	Severe
Single	58	7	6	1
Multiple	18	3	4	3
Total	76	10	10	4

however, the number of 22-gauge needles used in this sample was too small to draw valid conclusions.

All patients were satisfied with their anaesthetic and those who had a postdural pucture headache did not associate this with the type of anaesthesia received.

Discussion

Spinal anaesthesia is a common anaesthetic technique used for urological surgery, and it has been assumed by many anaesthetists that the use of relatively small gauge spinal needles (26-gauge) and the age of the patients involved in this type of surgery minimise the risk of postdural puncture headache. Our postoperative survey has shown that in our department there is a high incidence (24%) of these headaches and that 15% of patients suffer from moderate or severe headaches which last 12–24 h. The chance of developing a postdural puncture headache is significantly increased if more than one attempt at subarachnoid puncture is attempted. This suggests that tears or small holes are made in the dura but go unrecognised, possibly because of inadequate penetration of the subarachnoid space or the fine gauge of the needle which allows only a slow flow of cerebrospinal fluid back through the needle. Previous work [3] using the Sprotte 24-gauge spinal needle and comparing this with a 25-gauge Quincke tip needle, revealed no significant difference in the incidence of postdural puncture headache between the two groups. However, the Sprotte needle gave better puncture characteristics and as more than one attempt at dural puncture in our survey significantly increased the risk of postdural puncture headache we propose to investigate the use of the Sprotte needle in reducing these multiple attempts at dural puncture. Despite the high incidence of postdural puncture headache in our survey we found that all the patients were extremely satisfied and patients who had previously undergone general anaesthesia expressed a preference for spinal anaesthesia.

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Correspondence

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Shivering

In the editorial by Crossley (*Anaesthesia* 1992; **47:** 193–5), and in many similar articles by anaesthetists on shivering it is implied that the physiology of temperature regulation in animals is still unknown. However, it was fully, or almost fully, elucidated in the 1960s by physiologists and control system engineers alike and they are in agreement [1]. This knowledge makes peri-operative shivering more understandable, predictable and treatable.

Shivering is widely, and probably correctly, believed to occur due to loss of heat during long operations involving exposure, cold infusions and anaesthesia with rapid awakening. However, the association is suspect because a strict relationship with core temperature cannot be demonstrated. In fact, an animal's temperature set-point is quite variable in normal health. The temperature in the human core may be 35°C at rest in a cool environment in early morning, or 40°C during activity [2].

Temperature is regulated in an animal as it is in a large building, with predictive sensors detecting, not just absolute values, but rate of change [1], which gives a signal in keeping with expected heat loss or gain. The sensors are situated centrally, chiefly in the viscera, the spinal cord and hypothalamus, and externally, in the skin, particularly in the face in a hairless animal clothed normally, to detect thermal gradient [2]. In this way, heat production is stimulated in proportion to the steepness of the curve of heat loss and time, present and future. It is interesting to speculate upon the result of a system like this, with an output related

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to rate of change, such as going to sleep for an hour or two. A small temperature fall over this long time period may seem to have taken place instantly, producing an infinite rate of change and maximum heat production by mistake.

The signal from the surface sensors is necessarily reduced or ignored when core temperature is high and there is excess heat to dispose of. The skin temperature then is decreased by evaporation of sweat so that maximal blood cooling can occur in the vasodilated skin vessels, but shivering in response to this surface cooling would be inappropriate [2]. It follows that surface sensitivity to exposure to cold operating theatre draughts is increased if the core is already cool, so hypothermia in patients should be prevented. Many anaesthetists are familiar with the immediate benefit of applying heated blankets to stop shivering. The effect is too rapid to be due to core warming and must be due to quieting surface sensors and thermal gradient alarms. It should be remembered that the first effect of applying unheated blankets is surface cooling. It is unfortunate that there is never enough time for specialists to study other subjects. Engineers are familiar with the problems of designing systems and know that it is much easier to design them than analyse one made by another designer [1]. Control systems used in humans are frequently the same as control systems used by humans. It should be noted that of the 33 references in the extensive bibliography at the end of this editorial 29 were from anaesthesia journals, one from a physiology journal and none from the basic sciences.

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A reply

I thank Dr Potter for his interesting comments about my editorial. However, I must point out that at no point in the text did I state, or indeed imply, that the physiology of temperature regulation in animals is still unknown. I am aware of the extensive literature in this field and the reference which he quotes is an adequate review of physiological thinking on this subject as of 1980 [1]. The topic upon which I was asked to write was not, however, temperature regulation but peri-operative shivering, which explains the preponderance of references to anaesthetic studies in the bibliography. The question which is raised is whether the mechanisms of temperature regulation, which are well understood, are of major importance in the generation of peri-operative shivering, and as outlined in my text there is reason to believe that this may not be the case.

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Reference

[1] Hardy JD. Temperature regulation. In Mountcastle VB. *Medical physiology,* 14th edn, Vol. 2.

Chemical meningism after lumbar facet joint block

I wish to make two comments regarding the case report from Thompson *et al.*, (*Anaesthesia* 1991; **46:** 563–4). In their discussion, they state that application of polyethylene glycol in a 1:8 dilution to nerves, muscle and connective tissue has been shown to cause tissue necrosis. The reference they gave is that of Margolis *et al.* [1]. I wish to point out that this is a misquotation of their work. They did not in fact test polyethylene glycol at all, but propylene glycol, which is not a constituent of Depo Medrol (Depo Medrone in the UK), the preparation I assume was used, although neither the actual proprietary preparation nor its manufacturer is stated in this report. If the authors had actually read the original reports, this would have been quite evident to them and I must only assume that they were quoting from Nelson [2], who also made the same misquotation. My belief is that propylene glycol is quite a different substance to polyethylene glycol and is considerably more toxic [3].

The authors state that this patient developed meningism following a presumed intrathecal injection of 0.5% bupivacaine and methylprednisolone acetate. If this mixture was injected intrathecally, I wonder how the authors can explain the fact that the patient did not have any sign of a subarachnoid local anaesthetic block? Could it not be possible that the meningism was caused by the intrathecal puncture itself, possibly accompanied by a subarachnoid bleed?

I am certainly not attempting totally to discount the possibility that this patient developed chemical meningism due to the polyethylene glycol or methylprednisolone acetate preparation. However, I wish only to balance their report. Depo corticosteroids are often injected into the epidural space and there will always be a certain incidence of inadvertent subarachnoid injections. With care this can be minimised and most doctors working in this field would hate to lose this valuable pain relieving technique.

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A reply

We would like to thank Dr Berrigan for his comments. We confirm that the commercial preparation of methyl prednisolone acetate (MPA) used was Depo-Medrone (Upjohn Ltd), the constituents of which are stated in our case report.

Margolis *et al.* [1] investigated the long acting local anaesthetic efocaine; this contained as solvent both propylene glycol 78% and polyethylene glycol 2%. A similar anaesthetic and histological profile was demonstrated following application to tissues of either the efocaine solvent alone or 78% propylene glycol or the original preparation of efocaine [1, 2]. Chino *et al.* confirmed the neurotoxicity of 100% propylene glycol by perineural injections of rat sciatic nerves and suggested that propylene glycol may be useful for chemical neurolysis [3].

The literature on the subject of neurotoxicity of the various glycol solvents is confused by several authors, where the names propylene and polyethylene glycol are used interchangeably [4, 5]. Polyethylene glycol is a constituent of both Depo-Medrol (USA) and Depo-Medrone (UK). Propylene glycol has never been part of either of these formulations. Benzon *et al.* [6] tested the effects of 3–40% concentrations of polyethylene glycol on an *in vitro* rabbit sheathed and unsheathed nerve preparations. They found a reversible concentration dependant reduction in compound action potentials and conduction velocities that was statistically significant at concentrations greater than 10%. They concluded that solutions of 3% polyethylene glycol, as found in Depo-Medrone, did not affect nerve conduction and that polyethylene glycol in concentrations up to 40% did not cause neurolysis.

We can find no reference to the effect of polyethylene glycol on the meninges after intrathecal injection. The question remains whether the spinal fluid pleocytosis and increased protein content seen in patients with sterile meningism is a result of idiosyncracy either to mechanical puncture or chemical irritation due to the solvent, the steroid or, as suggested by Dr Berrigan, a small subarachnoid bleed. We postulated that our patient did not develop a subarachnoid block as only a small amount of our local anaesthetic and steroid mixture was injected before withdrawal of the needle. Chemical meningism is a clinical expression of an idiosyncratic reaction to foreign material in the subarachnoid space.

The US preparation Depo-Medrol has recently been reformulated by adding 0.9% benzyl alcohol as a preservative. Initially, anaesthetists were not informed, the company never having approved the formulation for spinal use. Both preparations have been retained on the market by Upjohn (USA). The company have no plans at present to introduce a benzyl alcohol containing form into the UK. In a recent plenary lecture entitled ‘Epidural steroids—still safe and effective after all these years?’ at the Pain society of Great Britain and Ireland, the literature was extensively reviewed. Although the evidence from clinical trials is inconclusive regarding efficacy, there is no doubt that clinicians find this a most valuable treatment modality which is not associated with severe side effects. Complications have been reported after intrathecal steroids and so careful technique especially in patients who have undergone previous spinal surgery is essential.

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Simplified quality of anaesthesia scoring system

The anaesthesia literature contains numerous articles comparing different anaesthetic techniques. Subjective criteria are typically used to assess the adequacy of anaesthesia. In many of these articles, anaesthetic conditions are described as ‘smooth,’ ‘too light’ or ‘too deep.’ In an attempt to provide for a more objective assessment of intra-operative conditions, Dr J. B. Glen (*Anaesthesia* 1991; **46:** 1081–94) has proposed a quantifiable scoring system. Although we would agree that there is a need for an objective scoring system to quantify anaesthetic conditions during the maintenance period, we found the proposed scoring system unnecessarily complicated. Therefore, we have proposed a simplified version of Glen’s quality of anaesthesia scoring system (Table 1). In addition, we have provided clinical data which demonstrates that the two scoring systems are comparable in assessing the anaesthetic conditions.

In a randomised, double-blind study comparing fentanyl and ketorolac when administered as analgesic adjuvants to a propofol–nitrous oxide anaesthetic technique in spontaneously breathing outpatients undergoing minor gynaecological procedures, we found that the ketorolac-treated patients required more supplemental fentanyl during the maintenance period (Table 2). In spite of the increased requirement for intra-operative ‘rescue’ (analgesic) medication, patients in the ketorolac group had

Table 1. Modified quality of anaesthesia scoring system.

(1)	*Movement in response to surgical stimulation*		
	None	☐ 0	
	Occasional mild responses (no interruption to surgery)	☐ 5	
	Frequent mild responses	☐ 10	
	Occasional marked responses (temporary interruption to surgery)	☐ 15	
	Frequent marked responses	☐ 20	
(2)	*Haemodynamic instability*		
	None (ΔMAP < 10% from baseline)		☐ 0
	Mild hypotension or hypertension (ΔMAP 10–20%)		☐ 2
	Moderate tachycardia (HR > 100) and/or hyper- or hypotension (ΔMAP) 20–30%		☐ 4
	Persistent marked tachycardia (HR > 120 and/or hypotension (ΔMAP > 30%))		☐ 6

Table 1. – *continued*

(3)	*Mean end-tidal CO_2 (mmHg)*	
	30–40	☐ 0
	40–50 or < 30	☐ 2
	50–60	☐ 4
	> 60 or assisted ventilation	☐ 6
(4)	*Recovery time from end of surgery to response to commands*	
	< 5 min	☐ 0
	5–10 min	☐ 5
	10–20 min	☐ 10
	20–30 min	☐ 15
	> 30 min	☐ 20

Total score———

Table 2. Demographic data for the two analgesic treatment groups†.

	Fentanyl	Ketorolac
Number; *n*	24	25
Age; year	41 (18)	39 (11)
Weight; kg	73 (13)	68 (15)
Surgery time; min	13 (11)	16 (11)
Anaesthesia time; min	26 (14)	29 (14)
Propofol induction; mg	74 (15)	77 (15)
Total dose; mg	242 (123)	268 (134)
Infusion rate; $\mu g.kg^{-1}.min^{-1}$	82 (126)	92 (85)
Supplemental fentanyl; μg	10 (28)	50 (69)*

*Significantly different from the fentanyl group, $p < 0.05$.
†Mean values (SD) or numbers.

Table 3. Quality of anaesthesia assessment scoring systems for the two analgesic treatment groups†.

	Glen system		Modified system	
	Fentanyl	Ketorolac	Fentanyl	Ketorolac
Movement	10.5 (2), 10	12.0 (2)*, 12	0.9 (3.3), 0	4.3 (4.6)*, 5
ΔMAP and ΔHR	0.2 (0.4), 0	0.6 (0.7)*, 1	0.4 (1.6), 0	1.2 (1.3)*, 2
$P_{E'}CO_2$	0.5 (0.8), 0	0.3 (0.6), 0	1.0 (1.6), 0	0.5 (1.1), 0
Awakening	0.5 (0.6), 1	0.3 (0.5), 0	2.7 (3.0), 5	1.5 (2.8), 0
Overall scoring	9.4 (2.5), 9	12.1 (3.4)*, 13	5.5 (4.8), 5	7.4 (5.3)*, 7

†Range: mean value (SD), and median scores.
*Significantly different from the fentanyl group, $p < 0.05$.

significantly higher movement and haemodynamic instability scores than those in the fentanyl group. Our results, using the simplified anaesthesia scoring system, were comparable to those obtained using the scoring system proposed by Glen (Table 3). Further studies involving other anaesthetic and analgesic drugs are needed to establish the utility of these two intra-operative scoring systems.

We would encourage other investigative groups to evaluate these scoring systems as tools for improving the quantification of anaesthetic techniques during comparative pharmacological studies involving anaesthetic and analgesic drugs.

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Use of calcium chloride for propranolol overdose

As an adjunct to the recent correspondence about propranolol overdose [1, 2] I would like to draw attention to a case report of severe propranolol overdose which responded dramatically to the administration of calcium chloride [3].

A fit, 22-year-old, 50 kg female presented with generalised seizures and sudden onset of electromechanical dissociation with sinus rhythm and broad QRS complexes. She had taken a large, unspecified quantity of propranolol and a smaller quantity of metoclopramide 1 h before. She was taking propronolol for a benign tremor and was receiving no other medication. Initial resuscitation with adrenaline, atropine, fluids and bicarbonate gave no response. Calcium chloride, however, repeatedly produced a dramatic restoration of blood pressure and a narrowing of the QRS complex. The calcium was administered in 1 g boluses, followed by an infusion of 0.08 $g.min^{-1}$ which was rapidly reduced to 0.005 $g.min^{-1}$ according to the ECG pattern and the blood pressure level. Neither isoprenaline, nor glucagon, nor more invasive methods of supporting the circulation, were required during her management.

Serum calcium has a direct effect on myocardial contractility because influx of extracellular calcium, as well as calcium from the sarcoplasmic reticulum, contribues to contraction of the myofibrils [4]. One of the metabolic manifestations of propranolol is hypocalcaemia, presumably through a blocking action on parathyroid hormone release [5, 6]. Parathyroid hormone has a short half-life and can rapidly alter serum calcium [7]. It is possible to conjecture that acute hypocalcaemia may have contributed to cardiovascular collapse in this case. It is interesting to note that calcium was not administered in either propranolol overdose reported in *Anaesthesia* [1, 2].

The Resuscitation Council of the United Kingdom has only recommended the use of calcium in electromechanical dissociation associated with hyperkalaemia, hypocalcaemia and calcium antagonist overdose [8]. Based on this case report I suggest that calcium may have a role to play in propranolol overdose.

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Anaesthesia in the neuroleptic malignant syndrome

A 15-year-old boy was admitted suffering an acute psychotic illness. Following treatment with chlorpromazine he became confused and developed a tachycardia (of 110 $beat.min^{-1}$) and a pyrexia of 37.5°C. Muscle tone of the jaw and trunk was noted to be increased. Neuroleptic malignant syndrome was suspected and serum creatinine phosphokinase (CPK) was measured at 5530 $IU.l^{-1}$ (normal range up to 195 $IU.l^{-1}$). The chlorpromazine was discontinued and sedation continued with lorazepam, but the patient remained suicidal.

One week after admission, anaesthesia for urgent ECT was requested. The patient was apyrexial and his muscle tone normal. The CPK was 762 $IU.l^{-1}$. For the first treatment atracurium 10 mg was administered followed after one minute by propofol 150 mg, and the patient's lungs were ventilated with 100% oxygen. Three minutes after the atracurium, the ECT stimulus was applied. This produced a marked degree of opisthotonus but the ensuing convulsion only lasted 15 s. A further stimulus was applied which produced a convulsion of 25 s. Increments of propofol were given to maintain anaesthesia until adequate recovery of neuromuscular function occurred. Reversal of the neuromuscular blockade was not attempted. Subsequent treatments employed a technique of incremental methohexitone and atracurium 15 mg followed by reversal after 10 min. This produced satisfactory anaesthesia, and adequately modified the tonic phase without prematurely shortening the clonic phase.

The neuroleptic malignant syndrome (NMS) is characterised by pyrexia, increased muscle tone, fluctuating level of consciousness, and autonomic dysfunction. The CPK is usually raised [1]. Death may result from hyperthermia and cardiovascular collapse, respiratory failure, or rhabdomyolysis, renal failure and coagulopathy [2, 3]. The pathophysiology of NMS is thought to involve central dopamine receptor blockade, and initiation of neuroleptics at high dosage may increase the risk of its occurrence. Treatment is supportive but the prognosis is improved if specific therapy employing dantrolene and/or bromocriptine is used. In the case described the condition was recognized early and specific therapy was not required. Complete withdrawal of neuroleptic drugs is essential and ECT may then be required to treat continuing psychiatric symptoms [4]. ECT has also been reported to improve the symptoms of NMS, possibly by increasing dopamine levels in the brain [5].

Despite earlier concerns, these patients are not at risk of developing malignant hyperthermia (MH) [3, 6]. Nevertheless, it is important that any anaesthetic technique employed for ECT does not produce dangerous complications, or jeopardise the effectiveness of the treatment. Suxamethonium may cause rhabdomyolysis and hyperkalaemia in the presence of active muscle disease. A competitive neuromuscular blocker will reduce muscle tone in NMS (whereas no effect is seen in MH) and should be used in adequate dosage to prevent the tonic phase causing musculoskeletal damage. Anaesthesia must then be maintained until reversal is possible. Propofol is known to shorten ECT induced convulsions and may increase the number of treatments required [7]. It is probably best avoided.

Anaesthetists need to be aware of the neuroleptic malignant syndrome, in the context of anaesthesia for ECT. The technique described above employing methohexitone and atracurium with subsequent reversal produced satisfactory results in this case.

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A hazard of heated humidifiers

I would like to remind colleagues of the need for vigilance when using heated humidified breathing systems. A 4-year-old girl presented for urgent revision of a blocked ventriculo-peritoneal shunt. Both the surgery and anaesthesia proceeded uneventfully, during which time the child's lungs were ventilated with a Servo 900C ventilator and a disposable breathing system. The inspired gases were warmed and humidified via a Bennet Cascade hot water humidifier, set to deliver gases at 37°C. At the end of the procedure the covering green towels were removed and it was noted that the breathing system had inadvertently been allowed to rest on the patient's feet, resulting in superficial burns and blistering (Fig. 1).

The risk of thermal injury to the airway from overheated breathing systems is well known, but the risk of burns from contact with the tubing is perhaps less obvious. In this case the humidifier was functioning correctly, delivering the preset temperature at the patient end of the system. However, because of the effect of cooling occurring along the system, which is enhanced by low minute ventilation, the temperature at the proximal end of the system is much higher, 46°C in this case. Clearly it is important that anaesthetists ensure that no part of heated systems be allowed to rest on patients.

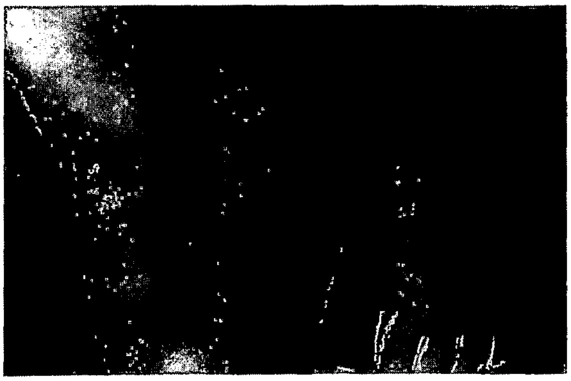

Fig. 1. Superficial blistering and surrounding erythema from heated breathing circuit.

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The hypnotic actions of alpha$_2$-adrenoceptor agonists

It was interesting to read the admonition voiced by Drs Aanta and Kanto concerning clonidine and the newer alpha$_2$-adrenoceptor agonists (*Anaesthesia* 1992; **47:** 533). We agree with them that the widespread use of this class of drugs as anaesthetic adjuncts may increase the incidence of awareness, given that their specific effects on the anaesthetic paradigm have not been fully elaborated. To date, the published literature reporting the anaesthetic-sparing effects of this class of drugs were based on indirect parameters of anaesthetic depth, such as attenuation of autonomic responses and haemodynamic end-points. It remains to be answered whether alpha$_2$-adrenoceptor agonists potentiate the hypnotic component of anaesthesia.

To resolve this important issue, future studies will need to measure anaesthetic depth directly. Since the middle latency waves of the auditory evoked potentials (MLAEP) have emerged to be the most promising indicator of anaesthetic depth [1–3], we felt that this modality represents the logical choice to confront the problem. Indeed, Thornton *et al.* have used MLAEP in combination with somatosensory evoked responses to differentiate the hypnotic and analgesic effects of nitrous oxide [4]. We have embarked on a study recently and our preliminary findings do suggest that clonidine potentiates anaesthetic depth as indicated by MLAEP parameters during isoflurane anaesthesia, in patients undergoing gynaecological procedures.

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Airway obstruction and the laryngeal mask airway in paediatric radiotherapy

We note the understandable enthusiasm for the use of the laryngeal mask airway (LMA) in conjunction with inhalational anaesthesia for the treatment of chidren undergoing radiotherapy. Indeed, this has formed the basis of our technique for the past 3 years.

However, we would like to highlight the airway problems that can occur, even with an apparently well-positioned LMA, when the patient is in the prone position with the head immobilised in a shell [1]. On 11 (3.5%) of the 313 occasions on which we have used this technique, serious airway obstruction has occurred, just after the patient had been positioned and thus at a time when the anaesthetist was still at hand to correct the obstruction. Five instances involved one child, in whom X ray eventually demonstrated marked kinking of the LMA in the oropharynx. In this child, the problem was solved by using an armoured LMA, which was on trial in the hospital.

It is interesting to compare this with our previous technique, in which we used a Guedel-type airway, adapted for insufflation [2]. During 525 such anaesthetics, we encountered airway obstruction on 11 (2.1%) occasions. Overall, therefore, using the LMA has not reduced the incidence of airway obstruction. However, in the Guedel airway group, two episodes of obstruction (detected by capnography) occurred during treatment, necessitating interruption of irradiation. This has not so far occurred using the LMA. Furthermore, it has proved much easier to undertake capnography with the LMA.

We wish to emphasise that, even using the LMA, the airway is still at special risk in children anaesthetised in the prone position. We look forward to the general availability of the smaller sizes of armoured LMA, which we hope will further reduce the incidence of airway obstruction.

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Laryngomalacia—a specific indication for the laryngeal mask?

A 5-month-old male infant was scheduled for laryngoscopy and bronchoscopy under general anaesthesia. He had presented with mild intermittent stridor but was otherwise healthy. There had been no apnoeic or cyanotic episodes and he had gained weight normally. Pre-operative examination was unremarkable except for a mild inspiratory stridor. Apropine 0.15 mg was given intramuscularly 1 h before anaesthesia.

It was proposed to induce and maintain anaesthesia with spontaneous respiration of halothane in oxygen, to spray the vocal cords with local anaesthetic and then proceed to microlaryngoscopy and rigid bronchoscopy. On arrival in the anaesthetic room the child was alert and breathing normally with minimal stridor. Venous access was established and induction commenced with halothane in oxygen. However, as soon as consciousness was lost, the stridor worsened. It became difficult to deepen anaesthesia and the patient's oxygen saturation fell from 95 to 80%. A steady state of light anaesthesia was reached but with an oxygen saturation of only 75–80%. A Guedel airway was tolerated but did not improve the situation. Anaesthesia could not be deepended further, nor was it possible to demonstrate chest movement on gentle manual ventilation.

At this stage it was considered expedient to abandon the plan to perform rigid endoscopy and instead undertake flexible endoscopy via a laryngeal mask airway. A size 2 laryngeal mask was inserted with immediate improvement in the airway. The stridor disappeared, the oxygen saturation increased to 98% and it became possible to demonstrate movement of the chest wall on manual ventilation. Anaesthesia was deepened easily and the surgeon proceeded to insert a fibreoptic nasendoscope (Olympus ENF type P3) through the laryngeal mask. An excellent view was obtained and the classical features of laryngomalacia could be demonstrated. Recovery from anaesthesia was uneventful.

This case illustrates the fact that infants with laryngomalacia can be difficult to anaesthetise. Severe cases are clearly a challenge, but even mild cases, such as our own, can cause problems. In our patient the use of the laryngeal mask was dramatically successful. It helped presumably by supporting the lax supraglottic tissues to prevent them from being drawn into the glottic opening.

The laryngeal mask has been advocated for diagnostic flexible bronchoscopy in children [1, 2] because it provides a clear airway and allows dynamic assessment of the airway and vocal cord movement during lightening of anaesthesia. We would suggest that it is of specific value in cases where laryngomalacia is a possibility.

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Spurious end-tidal CO_2 diagnosed by capnogram

We wish to report an atypical capnogram noted during an elective cranioplasty in a 15-year-old girl. Anaesthesia was induced with propofol, fentanyl and atracurium. The lungs were ventilated with nitrous oxide 70% and isoflurane 0.5% in oxygen using a circle CO_2 absorber system driven by a Manley Servovent ventilator. End-tidal CO_2 was measured from a connector attached to the tracheal tube using a Capnomac (Datex), a sidestream carbon dioxide

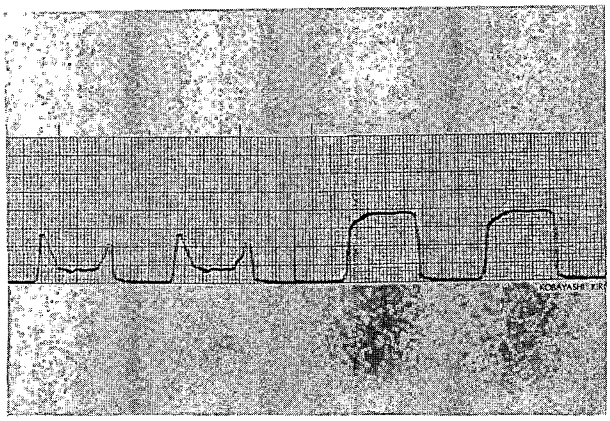

Fig. 1.

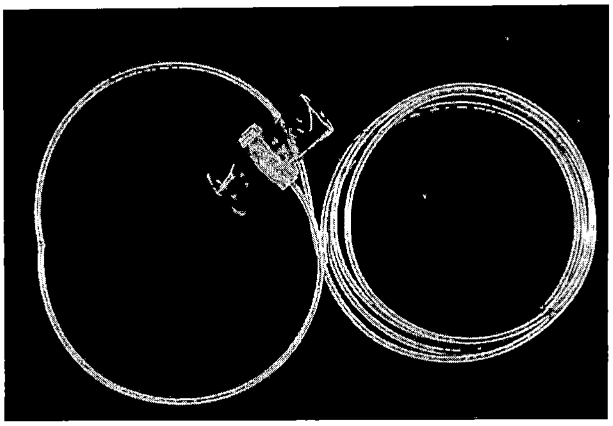

Fig. 2.

monitor which gives a digital display of end-tidal CO_2 without waveform. The aspiration flow was set at 200 ml.min^{-1}.

Thirty minutes into the operation, the end-tidal CO_2 descreased from 3.8% to 2.8% over 10 s. No other change in cardiovascular or respiratory variables was noted. Expired minute volume, airway pressure, end-tidal O_2 and N_2 concentration and oxygen saturation remained unchanged. Monitoring of neuromuscular block indicated a post-tetanic count of zero. An inspection of the breathing system did not reveal any fault and the possibility of venous air embolism was considered and appropriate action taken. Arterial blood gas analysis revealed a $P\text{aCO}_2$ of 4.1 kPa. At that stage, we were able to interface the Capnomac monitor to the Satlite (Datex) oximeter and display the end-tidal CO_2 waveform. The capnogram (Fig. 1) consisted of a plateau with two peaks.

A further assessment of the stiff perfusor tubing (B. Braun Melungen AG 874564/1) used for carbon dioxide sampling revealed a split (Fig. 2) where it must have been bent and damaged. When the hole was occluded, the capnogram waveform returned to normal and the end-tidal CO_2 was 4%. The split was only apparent when the tube was bent acutely and not when the tube lay naturally. Although the manufacturer's disposable sampling sets are recommended, improvisations may be necessary when the monitor must be placed far from the tracheal tube or when expense is a consideration.

The first peak of the plateau is the normal expected waveform and there is probably residual high pressure at the onset of expiration in the sampling system causing a small leak of expired gas through the hole. As the airway pressure decreases during expiration, there is entrainment of room air through the hole to dilute the sampled expiratory gas resulting in a lower plateau. The peak at the end of the plateau is probably the result of the positive pressure generated at the beginning of inspiration which reduces the amount of entrainment of room air. A peak at the end of the plateau has also been described when the surgeon leans on the patient's chest [1]. The degree of leak determines the height of the peak and plateau but the digital value displayed by the Capnomac will be closest to the plateau value. The possibility of a venous air embolism was disconcerting and this incident reaffirms the importance of having the capnogram displayed during carbon dioxide monitoring.

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Failure of an Ohmeda OAV 7750 ventilator

We describe how an Ohmeda OAV 7750 ventilator, which consists of an electronic control unit and a pneumatic drive unit, calibrated as a matched pair, failed to cycle. The pneumatic drive unit attaches to the bellows of the breathing cassette. The ventilator, mounted on an Ohmeda Excel 210 machine, and fitted with a rebreathing cassette and circle system, had just been installed; satisfactory machine and circuit checks were carried out before its use on each occasion.

During anaesthesia with IPPV for patients 8 and 9, it was noted that temporary arrests in ventilation, lasting approximately 20 s and 15 s, occurred, and before any intervention was made mechanical ventilation resumed normally. No alarms sounded, but on both occasions the expired minute volume decreased from 6.5 l to 4.5 l. Within 2 min of resumed ventilation the expired minute volume reached its original level. The lungs of the 10th patient were ventilated without incident. On the 11th occasion, pre-anaesthetic checks showed the ventilator to be nonfunctioning, together with the spirometer and oxygen analyser, and the low pressure alarm sounded, as described in the Service Manual [1].

The agents agreed that the hospital Biomedical Engineers should open the casing and inspect the ventilator. Inspection of the pneumatic drive unit showed that a brake unit-securing screw [2], holding a plate on which the brake unit cap was mounted, had loosened to such an extent that it had impinged on the cap; this had scored the metal and interfered with movement of the brake cap and hence the arm which actuated the bellows. Re-insertion and fixation of the screw was sufficient to allow the ventilator and monitors to function normally.

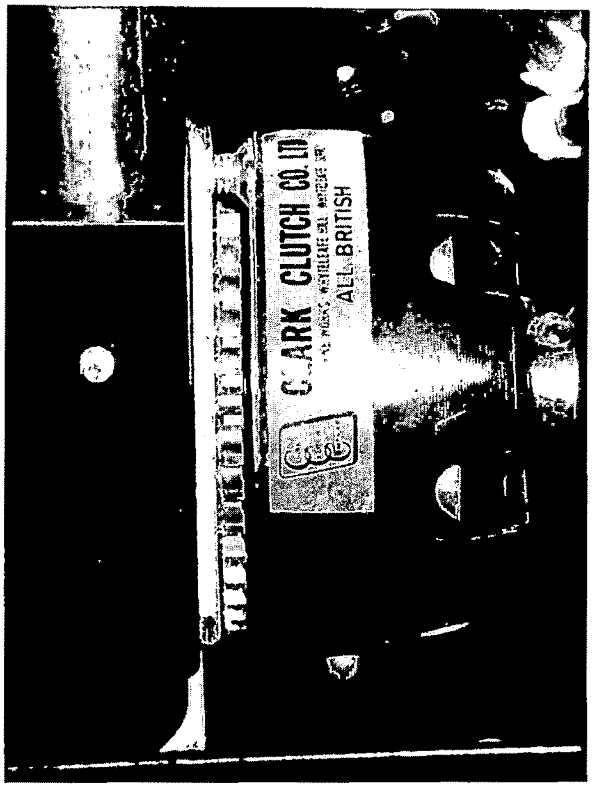

Fig. 1.

The photograph (Fig. 1), taken from the rear of the pneumatic drive unit, shows the offending screw contacting the brake cap. Scoring of the metal is visible.

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[1] OAV 7750 Anaesthetic Ventilator. Service Manual. BOC Health Care: 4.1. A. Start up routine.
[2] OAV 7750 Anaesthetic Ventilator. Service Manual. BOC Health Care: 7.12 Fig. 7.10 Brake/potentiometer unit, & 7.17 Fig. 7.13 Drive Cylinder.

Partial failure of a Servo 900C ventilator

I should like to report a bizarre malfunction which occurred on three separate occasions in a Siemens Servo 900C ventilator used in a paediatric intensive care unit.

The fault first presented when a 3-year-old child was being weaned from mechanical ventilation using the synchronised intermittent mandatory ventilation with pressure support (SIMV+PS) mode. The duty anaesthetist was alerted by nursing staff when the patient suddenly became restless, started ‘fighting the ventilator’ and developed an increased $Pa\text{CO}_2$ and reduced $Pa\text{O}_2$. Observation revealed obstructed inspiratory efforts interposed with normally synchronised IMV breaths. Inspection of the ventilator showed that all controls were set appropriately. The problem seemed to arise from an intermittent failure of the ventilator to trigger in response to the patient’s inspiratory efforts. On approximately every third spontaneous breath the airway pressure was noted to swing 15–20 cmH$_2$O negative to atmospheric pressure before any gas was supplied to the patient circuit. Another Servo C ventilator was substituted and weaning continued uneventfully using the SIMV+PS mode.

The original ventilator was given a full on-site service by a Siemens engineer. It was passed as functioning normally and returned to service. A few days later the same fault recurred when the ventilator was used in the SIMV+PS mode. The clinical presentation was similar to the first. This time the nature of the fault and the fact that it occurred only with the combination of SIMV+PS was demonstrated to Siemens’ service personnel by breathing through the ventilator via a clean patient circuit. The ventilator was taken for a complete factory service and was returned a few weeks later. On this occasion the machine was checked before use by breathing through it to confirm that it functioned correctly in all SIMV combinations.

However, after performing satisfactorily in both controlled mechanical ventilation (CMV) and SIMV+PS modes for about 4 weeks the same fault recurred abruptly. On this occasion the staff were alerted immediately by the patient complaining that it had become ‘harder to breath’ and that the machine was not giving her any air when she took a breath!

Inspection of the ventilator confirmed that the CMV, CPAP and pure Pressure Support modes all functioned normally but that an intermittent failure to trigger on spontaneous breaths was present with the SIMV+PS mode selected. The normal functioning of the other modes, which employ the same electromechanical valves and flow and pressure transducers as the SIMV+PS mode, suggested that the fault lay in the control hardware or software rather than in the ‘peripheral’ components. This was demonstrated to a senior technical representative from Siemens and subsequent investigation of the control system revealed that the fault lay in one of the electronic circuit boards. This was replaced and the ventilator has subsequently functioned without problems. Fortunately none of the patients suffered harm as a result of the ventilator malfunction.

This account demonstrates that it is possible for sophisticated electronically controlled machines to suddenly develop highly selective faults which may be very difficult to locate and repair. An additional problem is that such a fault may compromise the safe functioning of the equipment without immediately triggering an alarm. This incident underlines once again the importance of continuous clinical observation of any patient who is critically dependent upon mechanical devices.

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A reply

Thank you for the opportunity to reply to Dr Sanders' letter.

This ventilator had a very intermittent fault, which was only reproduced after extensive testing in our medical electronics workshop. When reproduced, the fault was immediately corrected. The Servo ventilator 900C has operator set alarms which are independent of the ventilation control system. The expired minute volume alarm will activate promptly in the event of conditions deviating from the range set by the operator.

We wholeheartedly agree with Dr Sanders' statement regarding the importance of continuous clinical observation of any critically dependent patients.

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Ventilators, circle systems and respirometers

I wish to draw attention to a potential problem with interpretation of tidal volumes displayed by respirometers. It is customary for respirometers to be placed in the expiratory limb of a circle system. If a patients lungs are ventilated by a Nuffield 400 ventilator, the respirometer will, in this position, display full tidal volumes despite the inspiratory limb being disconnected. This is because the downward filling bellows are expanded by gravity, and generate a negative pressure as they fill. This sucks air in through the expiratory limb. Ventilators with upwards filling bellows do not generate a negative pressure, and this problem does not arise.

The assumption that volumes displayed are delivered to the patient could be wrong in the case of a disconnection. Although other monitors such as ventilator alarms and end-tidal carbon dioxide monitors should alert anaesthetists in this event, those of us who use this system should be aware of its limitations.

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A reply

Thank you for the opportunity to reply to Dr Thorpe's comments.

The limitations of using a spirometer as a breathing system disconnect monitor are indeed highlighted in Dr Thorpe's letter and should serve as a caution to users of all descending bellows type of ventilators not just the NV400. This clearly demonstrates the need for the user to consider carefully the application and select the monitor that will best suit the particular installation, a situation more difficult in breathing systems because of the need to ensure that there is sufficient gas flow (in the correct direction), sufficient pressure is generated, there is no leak (split hose) and there is no disconnection of the tapers.

The use of a breathing system pressure monitor such as the IDP alarm is generally considered to provide a better indication of breathing system disconnection than a spirometer, specifically for the reasons identified above.

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Pulmonary oedema due to fentanyl?

We present a previously healthy patient who developed acute pulmonary oedema after administration of fentanyl plus atropine. This is an unusual adverse reaction which, to our knowledge, has not been reported previously.

The patient was a 27-year-old healthy male who smoked 40 cigarettes per day. He was scheduled for surgery for a carpal tunnel syndrome under general anaesthesia. Immediately after intravenous fentanyl 100 μg and atropine 0.5 mg he became agitated, with a tachycardia of 115 beat.min^{-1}, dyspnoeic, hypotensive (blood pressure 100 mmHg); his oxygen saturation decreased to 80% and he complained of abdominal pain. These symptoms were thought initially to be due to anxiety, and hence anaesthesia was combined with propofol 200 mg and atracurium 40 mg. When the trachea had been intubated a reddish secretion appeared from the tracheal tube. The clinical picture now progressively deteriorated, with severe hypotension (arterial blood pressure 60 mmHg) increasing hypoxemia (oxygen saturation 70%) and tachycardia (130 beat.min^{-1}). Auscultation revealed rales throughout the lung fields and a diagnosis of acute pulmonary oedema was made.

Surgery was postponed and the patient woke up a few minutes later; he was dyspnoeic, cold, sweaty and was coughing up blood-stained, frothy sputum. Chest X ray showed vascular congestion and diffuse pulmonary infiltrates; the cardiac silhouette was normal. The diagnosis of noncardiogenic acute pulmonary oedema was confirmed. Frusemide 40 mg was given with good effect. Thirty minutes later, all symptoms and signs of acute pulmonary oedema had resolved. His blood pressure was 120/80 mmHg, pulse rate 70 beat.min^{-1} and respiratory rate 22 min^{-1}. Arterial blood gases showed pH: 7.40; $P\text{CO}_2$: 5.5 kPa; $P\text{O}_2$: 9 kPa and HCO_3 26 mmol.l^{-1}. All other laboratory investigations were normal. Due to the immediate temporal relationship between the development of acute pulmonary oedema and the administration of fentanyl and atropine, we believe that the observed events in this patient were related to one or both of these drugs.

Atropine has been used for very many years and no instance of pulmonary oedema in healthy subjects has been reported following its use. Although fentanyl-induced pulmonary oedema has not been described previously, noncardiogenic pulmonary oedema is a well-known complication after morphine [1], diamorphine [2], methadone [3], propoxyphene [4], naloxone [5] and nalbuphine [6]. In view of this we think that the pulmonary oedema in this patient was probably caused by fentanyl rather than by atropine.

Although the pathogenesis of noncardiogenic pulmonary oedema caused by opioids is unclear, available evidence suggest that there are alterations in the permeability of alveolar and capillary membranes, probably caused by mediators (leukotrienes and histamine) rather than elevation of pulmonary capillary pressure [7].

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Atrial fibrillation after electroconvulsive therapy

Most arrhythmias following electroconvulsive therapy are benign. We describe a patient in whom atrial fibrillation occurred immediately after such treatment.

An 84-year-old man with a depressive illness had had uneventful bimonthly electroconvulsive treatments as an outpatient for 4 years. His medical history was remarkable only for treated mild hypertension and benign prostatic hypertrophy. His blood pressure was 150/80 mmHg and pulse rate 70 beat.min^{-1}. Electrocardiographic and chest X ray findings were normal. Atropine 0.4 mg was given intramuscularly as premedication. After a blood-pressure cuff, pulse oximeter and electrocardiographic monitors had been placed, he was given methohexitone 60 mg and suxamethonium 60 mg. When adequate relaxation was achieved, assisted ventilation was begun and bilateral electroconvulsive therapy administered.

Immediately afterwards, a supraventricular tachycardia developed, associated with a heart rate of 180 beat.min^{-1} and blood pressure of 170/100 mmHg. Esmolol 25 mg was given intravenously in incremental doses, which reduced the heart rate to 120 beat.min^{-1} and blood pressure to 160/90 mmHg. Oxygen saturation was stable at 96%, but telemetry indicated an irregular rhythm. Electrocardiography showed atrial fibrillation and a ventricular response of 120 beat.min^{-1}, which persisted for 20 to 30 min. The patient, now alert, had no chest pain, shortness of breath, or general discomfort. Cardioversion using 100 Joules was performed after administration of methohexitone 50 mg. A normal sinus rhythm of 80 beat.min^{-1} resulted. The patient was observed for 3 h and then discharged home. Esmolol 20 mg intravenously was used prophylactically during subsequent electroconvulsive treatments, and no abnormalities were observed.

Cardiovascular complications cause most of the medical problems and deaths in patients undergoing electroconvulsive therapy [1]. Transient benign arrhythmias occur more often in elderly patients and patients with cardiac disease [1, 2] and in association with hypoxaemia, or hypercapnia [3]. The pathophysiological changes due to the ECT may render high-risk patients susceptible to arrhythmias. A brief vagal response is followed by a burst of sympathetic activity accompanying the seizure. This activity can predispose compromised patients to myocardial ischaemia or stretching of atrial fibres, resulting in atrial fibrillation [4]. Studies in animals have shown that electrical stimulation of the brain can produce sympathetic-mediated arrhythmias, including atrial fibrillation [5]. We have found only one other report of atrial fibrillation associated with electroconvulsive therapy [6]. The treatment was administered without ECG monitoring and atrial fibrillation was detected 30 min later; the arrhythmia was attributed to an idiosyncratic response to suxamethonium.

Therapeutic and prophylactic efforts have focused on controlling the atrial and ventricular rates before ECT. One study found that labetalol was superior to esmolol in protecting against increases in heart rate and blood pressure [7], but that it significantly decreased seizure duration [7, 8]. Studies of the effect of esmolol on seizure length have yielded conflicting results [7, 8]. There have been no investigations of prophylaxis for supraventricular arrhythmias due to electroconvulsive therapy.

We considered our patient's arrhythmia to be an isolated phenomenon unrelated to underlying cardiac disease. We treated him with cardioversion instead of drugs because we assumed that his atrial fibrillation was due directly to the haemodynamic derangements resulting from the ECT. Furthermore, he was an outpatient who did not necessarily require admission for control of atrial fibrillation.

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Are the hazards associated with glass syringes justified?

Doctors Grover and Heath describe the inadvertent administration of a massive intravenous overdose of papaveretum when the glass syringe of a patient-controlled analgesia machine disengaged from the drive mechanism (*Anaesthesia* 1992; **69:** 402–4). The authors suggest that the reduced friction of the plunger in a glass syringe may have increased the likelihood of syphoning in unfavourable conditions. They state that one of the advantages of glass syringes is that they are more suitable than plastic for prolonged contract with drug solutions.

We would like to make two points. Firstly, the evidence of drug adsorption is varied. The authors refer to investigations done with fentanyl [1], where concentrations decreased by 11% in PCA reservoirs within the first few hours. This is supported by more recent work showing loss of drug [12.6%) in solution in polyvinyl chloride bags within 3 days of mixing [2]. On the other hand, it has been demonstrated that fentanyl concentrations remain stable over a 30 day period of sampling from portable pump reservoirs [3]. Work in our department confirms this stability; fentanyl citrate concentrations in 500 ml polyvinyl bags containing 0.9% sodium chloride showed no decline over a 14 day sampling period. Secondly, the main active constituent of the drug used by the authors is morphine and this does not share the characteristics of fentanyl. Morphine is less fat soluble and might be expected to be adsorbed to a lesser extent than fentanyl. Indeed, our own work has shown that when morphine is diluted in 50 ml syringes containing 0.9% sodium chloride, no reduction from initial concentrations over a 14 day sampling period occurs [4].

In view of this, and the other case report cited by the authors, where a cracked syringe barrel lead to a large bolus of morphine draining into a patient [5], we feel strongly that the substitution of glass for plastic syringes for drug infusions cannot be justified on grounds of drug stability.

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Nalbuphine—an analgesic with unique built-in safety feature

We wish to report an incident which demonstrated the ceiling respiratory depressant effect of nalbuphine [1], and enhanced our understanding of the drug. Nalbuphine is a kappa receptor agonist-antagonist analgesic equal or superior to fentanyl [2], morphine [3] and pethidine [4], with fewer emetic effects [3, 4]. It is reversed by naloxone [5].

A 10-year-old, 27 kg boy underwent an emergency appendicectomy; no premedication was given. Anaesthesia comprised pre-oxygenation, crash induction using thiopentone 125 mg, suxamethonium 50 mg, and cricoid pressure. Atracurium 15 mg and nalbuphine 5 mg were given after the suxamethonium had worn off. Anaesthesia was maintained with nitrous oxide and isoflurane in oxygen; the lungs were ventilated and routine monitoring used. The surgery lasted 38 min. Residual relaxation was reversed with neostigmine and atropine, and spontaneous respiration re-established. The child, however, did not rouse, so he was transferred to the recovery room where, despite adequate respiration and $Sp\text{o}_2$, he remained asleep with the tracheal tube *in situ*. To hasten rousal, return of reflexes and tracheal extubation, doxapram 20 mg was given, but there was no effect over the next 10 min; naloxone 0.02 mg was then given. When this failed to rouse the child, the dose was repeated, also without effect. An ampoule check then revealed that two ampoules of nalbuphine (20 mg each) had been administered instead of two ampoules of naloxone. The error was contributed to by the ampoules being packaged by the same manufacturer (Dupont) in boxes of the same size and colour, with similar ampoule blue/green colour coding.

Despite 40 mg of intravenous nalbuphine (about 15 times the recommended dose) the child's respiration and $Sp\text{o}_2$ were unaffected, which would undoubtedly have happened with the equivalent dose of morphine (40 mg). On discovering the error, naloxone 0.4 mg was given. Within minutes the child woke up, coughed, and his trachea was extubated. After an hour of observation in recovery, he was returned to the ward and nursed intensively overnight. No untoward effects of the nalbuphine overdose were observed.

Three aspects are noteworthy. Firstly, doxapram did not reverse the sedation produced by the induction dose of nalbuphine. Secondly, the massive dose of nalbuphine, without subsequent apnoea, confirmed to us its claimed ceiling respiratory depressant effect, a unique safety feature of this drug. Thirdly, the subsequent rousal produced by naloxone indicates that this is the agent of choice in the event of nalbuphine-induced sedation. These latter two safety aspects, combined with the reports of others and our own observations of its analgesic efficacy, have encouraged our continued use of nalbuphine as adjuvant for in-patient anaesthesia.

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A fasted patient?

Instructions about fasting and its duration are often poorly understood by patients. I would like to present one patient who presented with problems of regurgitation by her interpretation of the fasting rule.

Two months after undergoing successful renal transplantation, a 19-year-old, 63 kg female student was anaesthetised for removal of a ureteric stent. She had no gastrointestinal symptoms, and previous general anaesthetics were uneventful. Anaesthesia was induced with propofol 200 mg and a size 3 laryngeal mask airway (LMA) was inserted. Anaesthesia was maintained with nitrous oxide and 2% isoflurane in oxygen with spontaneous ventilation and was uneventful until the patient's legs were placed in the lithotomy position, whereupon she developed severe laryngospasm and colourless fluid poured from both nostrils. After oropharyngeal suction and removal of the LMA, suxamethonium was administered and the trachea intubated. Subsequent anaesthesia and recovery was uneventful, but a total of 500 ml of clear, viscous fluid of neutral pH was aspirated from the pharynx peri-operatively. A clue to the cause was provided by the operating theatre porter who had noticed a large pile of chewed gum on the patient's bedside locker. She had been chewing this during most of the 4 h period of pre-operative fasting and this had presumably stimulated profuse secretion of saliva. The nursing staff had noticed the patient was chewing gum, but had not thought this to be a problem.

The half-life of water in the stomach is only 12 min [1] and recent studies have shown no increase in residual gastric volume or in the incidence of regurgitation when clear fluids are administered 90–120 min prior to anaesthesia [2–4]. However, a combination of pre-operative anxiety causing reduced gastric emptying, and salivary gland stimulation from the continuous gum chewing throughout the fasting period, presented a serious anaesthetic risk in this patient.

It would seem worthwhile therefore to remind patients that the chewing of gum is prohibited by the fasting rules and to ensure that nursing staff appreciate this.

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Sugi absorbent swabs, dacrocystorhinostomy and partial respiratory obstruction

A 66-year-old, healthy, female patient presented for dacryocystorhinostomy (DCR) under general anaesthesia. A cuffed tracheal tube was used to secure the airway. At the end of surgery, which lasted 2 h, neuromuscular blockade was reversed. Pharyngeal toilet was carried out and the patient's trachea extubated once adequate spontaneous respiration was achieved. Shortly after extubation the patient experienced a sense of choking and mild inspiratory stridor. Laryngoscopic examination revealed one of the eye-swabs (Fig. 1) to be stuck between the vocal cords. The apex of the Sugi swab was directed toward the trachea and the base between the cords. It was retrieved using Magill's forceps and the respiratory obstruction was relieved. The rest of the postoperative period was uneventful.

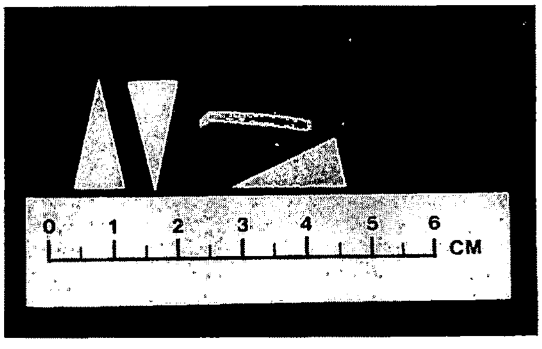

Fig 1.

The Sugi absorbent swab, which is made out of cellulose, can swell up 10–15 times its own weight on absorbing blood and secretions. The offending swab presumably had been left behind in the nasopharynx at the end of surgery. After extubation, the spontaneous respiratory efforts would have propelled the swab to the glottic region. Had it entered the tracheobronchial tree, it could have led to the obstruction of one of the smaller bronchi, with pulmonary collapse and infection. As the swab is radiolucent, the exact cause of the postoperative chest problem would have been missed.

This case illustrates the importance of getting the surgical team to account for all the Sugi swabs used during DCR.

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Pulse oximeter and Allen's test

I read with interest Dr Persson's letter on the use of the pulse oximeter and Allen's test (*Anaesthesia* 1992; **47:** 451). At least four other authors have described this approach using either a pulse monitor [1, 2] or pulse oximeter [3, 4]. In all four of these descriptions, as with that of Dr Persson, a hypothesis was formulated which was neither confirmed nor refuted by experimental evidence. When Dr H. M. Jones and myself compared these methods against the Doppler ultrasound [5] we found that the pulse monitor and the pulse oximeter techniques failed to detect the absence of an ulnar artery. I must therefore disagree with the conclusion reached by Dr Persson that an unchanged oxygen saturation reading should confirm adequate ulnar collateral flow.

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An unusual cause of motion artefact during pulse oximetry

Poor signal quality due to excessive movement of the probe site during pulse oximetry is well recognised, and occurs commonly in the presence of tremor. At our hospital, vascular surgery is usually performed under regional anaesthesia, with the patient awake. These procedures are often prolonged, and we provide the patient with a portable tape-recorder and headphones so that they can listen to music during the operation. We have found that a common cause of poor quality pulse oximetry is the rhythmical tapping of the patients fingers in time to the music. Transfer of the probe to the ear is inappropriate due to the presence of the headphones. Imperfect oximetry may therefore have to be accepted in this situation in order to ensure a relaxed, contented patient.

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'And where does the time go during operating lists?'

Ms J. Turner (*Anaesthesia* 1992; **47:** 69–70) is to be commended on her self-appraisal, honesty and also her courage in voicing her appreciation of her anaesthetist colleagues, a still fairly uncommon thing, even in the UK. I suspect that her letter would not have been published so readily in a surgical journal.

She raises some interesting points. Contrary to her opinion, I am sure I am not alone in sharing the view that regular allocation of lists is not dull, unless of course someone with whom one works is incompatible, and then it isn't dull either, from a negative viewpoint. It leads to efficiency and a pleasant working relationship, and usually therefore an optimum outcome for patients. In most hospitals, planning of a variable rota by the Anaesthetic Department one or two weeks ahead seems to be the norm.

Probably the most important point which Ms Turner has overlooked is that in many hospitals surgeons issue their operating lists late, the evening before or even on the same day of operating, making it difficult or impossible to assess the patients pre-operatively, leading to the possibility of otherwise avoidable complications and certainly cancellations and postponements, as patient safety is paramount. If pre-anaesthetic clinics were instituted as the norm, both day cases and elective and scheduled cases would be better screened, giving optimum conditions for patient safety, reducing wastage of precious operating theatre time, treating more patients and ultimately, of course, saving money.

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Anaesthesia, 1992, Volume 47, pages 918–919

Obituaries

Wilson, Henry Lister Llewelyn, MB, ChB, formerly Consultant Anaesthetist Gwent Health Authority. Qualified from University of Leeds in 1936.

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Harrison, Gwendolen, FFARCS, formerly Consultant Anaesthetist, Leeds General Infirmary. Qualified from University of Leeds in 1932.

International congress calendar

1992

1–2 October. London. *Continuing Medical Education and Training in Europe: the future.*
Information: Dr W.M.N. Nicholls or Mrs J.M. Coops, The Conference Office, c/o The Fellowship of Postgraduate Medicine, 6 St Andrew's Place, London NW1 4LB.

8–10 October. Mainz, Germany. *13th International Congress on Computers in Critical Care and Pulmonary Medicine.*
Information: Professor W. Dick, Klinik fur Anathesiologie, Langenbeckstrabe 1, Postfach 3960, 6500 Mainz, Germany.

17–20 October. New Orleans. *American Society of Anesthesiologists Annual Meeting.*
Information: Executive Secretary, ASA, 515 Busse Highway, Park Ridge IL 60068, USA.

4–6 November. Israel. *The Sixth International Symposium on Anesthesia and Intensive Care.*
Information: Dr A. Fisher, Division of Anesthesiology, Soroka Medical Center, Beer-Sheva 84101, Israel.

20–21 November. Brighton, England. *1st CPR Congress of the European Resuscitation Council.*
Information: Dr D.A. Zideman, Department of Anaesthesia and Critical Care, Hammersmith Hospital, Du Cane Road, London W12 0HS.

21–22 November. Philadelphia, Pennsylvania. *The Robert D. Dripps Memorial Conference: Defining the State of the Art in Anesthesiology.*
Information: Janice Ford, Hospital of the University of Pennsylvania, 1, Silverstein Building, 3400 Spruse Street, Philadelphia, PA 19104, USA.

10–11 December. Paris, France. *Conference de Consensus: Antibiotic Prophylaxis in Surgical Environment.*
Information: SOCFI, 14 rue Mander-75002, Paris, France

12–16 December. New York. *46th Postgraduate Assembly in Anesthesiology.*
Information: Kurt G. Becker, Executive Director, The New York State Society of Anesthesiologists, Inc., 411 East 42nd Street, Suite 1605, New York 10017, USA.

1993

16–23 January. Cancun, Mexico. *11th Annual Symposium, Clinical Update in Anesthesiology.*
Information: George Silvay, WACTVA, 1408 Madison Avenue, Suite 2C, New York, NY 10029, USA.

22–23 January. Leuven, Belgium. *Anesthetic Mishaps.*
Information: Prof. Dr H. Van Akenh, Department of Anesthesiology, University Hospitals K.U. Leuven, Herestraat 49, B-3000 Leuven, Belgium.

29–31 January. Anaheim, California. *31st Clinical Conference in Pediatric Anesthesiology.* Disneyland Hotel, 1150 West Cerritos Avenue, Anaheim, California 92802, USA.
Information: David J. Steward, MB, Program Director, Pediatric Anesthesiology Conference, Children's Hospital, Los Angeles, PO Box 54700, Los Angeles, CA 90054, USA.

30 January–6 February. Aspen, Colorado. *New Horizons in Anesthesiology.*
Information: Miss Kathleen A. Maitland, Department of Anesthesiology, Emory University at Crawford Long Hospital, 25 Prescott Street, 5404 Glenn, Atlanta GA 30308, USA.

12–16 February. Utah. *38th Annual Postgraduate Course in Anesthesiology—'Anesthesiology: Today and Tomorrow'.*
Information: Vicky Larson, Department of Anesthesiology, University of Utah School of Medicine, 50 North Medical Drive, Salt Lake City, Utah 84132, USA.

12–15 March. Hong Kong. *7th Congress of the Western Pacific Association of Critical Care Medicine.*
Information: Secretariat, International Conference Consultants Ltd. Suites A & B, 16th Floor Casey Building, 38 Lok Ku Road, Sheung Wan, Hong Kong.

14–18 March. Cape Town, South Africa. *South African Society of Anaesthetists Jubilee Congress.*
Information: Mrs S. Elliot, Postgraduate Education Centre, UCT Medical School, Observatory 7925, Cape Town, South Africa.

19–20 March. Brussels. *Second European Congress on Ambulatory Surgery.*
Information: Cl De Lathouwer, M.D. Brussels One Day Clinic, avenue du Duc Jean 71–73, B-1080 Brussels, Belgium.

19–23 March. San Diego, California. *67th Congress of the International Anesthesia Research Society.*
Information: Anne F. Maggiore, Executive Director, International Anesthesia Research Society, 2 Summit Park Drive, Suite 140 Cleveland, Ohio 44131, USA.

23–26 March. Brussels. *International Symposium on Intensive Care and Emergency Medicine, Brussels Congress Centre.*
Information: Secretariat, Professor J. L. Vincent, Department of Intensive Care, Erasme University Hospital, Route de Lennik 808, B-1070 Bruxelles, Belgium.

26–27 March. Euroanaesthesia 1993. *Quality Assurance in Clinical Anaesthesia.*
Information: IFAI Institut fur Anasthesiologie und Intensivbenhandlung, Inselspital, CH-3010, Bern, Switzerland.

21–23 April. Sheffield. *Anaesthetists in Training Annual Scientific Meeting and Linkman Conference, Octagon Centre, Sheffield.*
Information: The Honorary Secretary of the Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

29 April–2 May. North Carolina. *Meeting of the Association of University Anesthetists.*
Information: Franic M. James III, Department of Anesthesia, Wake Forest University Medical Center, 300 S Hawthorne Road, Winston-Salem, North Carolina 27193, USA.

13–16 May. Seattle. *American Society of Regional Anesthesia, 18th Annual Meeting, Refresher Course, Workshops.*
Information: ASRA, P.O. Box 11086, Richmond, VA 23230-1086, USA.

10–13 June. Boca Raton, Florida. *Annual Meeting of the Florida Society of Anesthesiologists.*
Information: Florida Society of Anesthesiologists, 6501 25 Way S. Ste D, St Petersberg, FL 33712, USA.

2–5 September. Porto, Portugal. *Annual Meeting of the European Academy of Anaesthesiology.*
Information: Dr Silva-Araujo, Director do Servico D Anesthes, Hospital Geral de Sto Antonio, Porto, Portugal.

1–4 September. Liverpool. *European Course and Congress in Paediatric Anaesthesia.*
Information: Dr P.D. Booker, Alder Hey Hospital, Liverpool L12 2AP.

11–18 September. *Second Anaesthesia and Critical Care Symposium (in Ireland). Sponsored by Yale University School of Medicine and the Royal College of Surgeons in Ireland.*
Information: Office of Postgraduate and Continuing Medical Education, Yale University School of Medicine, 333 Cedar St. New Haven CT, USA.

21–24 September. Ghent. *Update in Cardiac Surgery, Anesthesia and Intensive Care, 2nd Meeting.*
Information: Eric Mortier, University Hospital Ghent, De Pintelaan 185 B-9000 Ghent, Belgium.

22–24 September. Glasgow. *Linkman Conference and Annual Scientific Meeting. Joint Meeting between the Association of Anaesthetists of Great Britain and Ireland, and the Canadian Society of Anaesthetists.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

9–13 October. Washington DC. *American Society of Anesthesiologists Annual Meeting.*
Information: Executive Secretary, ASA 515 Busse Highway, Park Ridge, IL 60068 USA.

1994

15–18 March. Brussels. *14th International Symposium on Intensive Care and Emergency Medicine, Brussels Congress Center.*
Information: Secretariat, Professor J.L. Vincent, Department of Intensive Care, Erasme University Hospital, Route de Lennik 808, B-1070 Bruxelles.

7–10 April. Chicago. *American Society of Regional Anesthesia 19th Annual Meeting, Refresher Course, Workshops.*
Information: ASRA P.O. Box 11086, Richmond, VA 23230-1086, USA.

24–27 April. Montreal, Canada. *16th Annual Meeting and Workshops Society of Cardiovascular Anesthesiologists.*
Information: SCA, P.O. Box 11086, Richmond, VA 23230-1086, USA.

7–9 September. Brighton. *Linkman Conference and Annual Scientific Meeting.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

8–11 September. Hamburg, Germany. *Annual Meeting of the European Academy of Anaesthesiology.*
Information: Professor Schulte am Esch, Abt. F. Anaesthesiologie, Univ.-Krankenhaus, Eppendorf. Martinistr. D-2000, Hamburg 20. Germany.

2–7 October. Jerusalem. *European Congress of Anaesthesiology.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

1995

7–10 May. Pennsylvania. *17th Annual Meeting and Workshops Society of Cardiovascular Anesthesiologists, Philadelphia, Pennsylvania, USA.*
Information: SCA P.O. Box 11086, Richmond, VA 23230-1086, USA.

24–27 August. Helsinki, Finland. *Annual Meeting of the European Academy of Anaesthesiology.*
Information: Professor Tammisto, Dr Korttila, Helsinki University Central Hospital, Women's Clinics, Department of Anaesthesia, Haartmaninkatu 2, SF-00290, Helsinki, Finland.

13–15 September. Birmingham. *Linkman Conference and Annual Scientific Meeting.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

1996

5–8 May. Utah, USA. *18th Annual Meeting and Workshops Society of Cardiovascular Anesthesiologists. Salt Lake City.*
Information: SCA P.O. Box 11086, Richmond, VA 23230-1086, USA.

10–13 September. Harrogate. *Linkman Conference and Annual Scientific Meeting.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND

APPLICATION FOR MEMBERSHIP

to

The Association of Anaesthetists of Great Britain and Ireland
9 Bedford Square
London WC1B 3RA, England

(This application will be considered by Council at its next meeting. NO MONEY should be sent in the meantime. After acceptance of the application by Council, the Hon. Secretary will notify the applicant of Council's decision and the amount of subscription payable in the current financial year).

.... 19

The Honorary Secretary
Association of Anaesthetists of Great Britain and Ireland

I (full name) .... offer my name as a candidate
BLOCK LETTERS
for (a) ORDINARY MEMBERSHIP (b) OVERSEAS MEMBERSHIP (c) ASSOCIATE MEMBERSHIP (d) TRAINEE MEMBERSHIP of the Association *(please delete categories not applicable)**

I hold the following appointment(s) as an anaesthetist *(please state grade if in National Health Service, and indicate the approximate proportion of time spent in the practice of anaesthesia)*:

....

....

....

Qualifications (with dates)..

....

(Signed) ....

Address ....

.... Hospital Tel. No: ....

.... Home Tel. No: ....

We, being Members† of the Association, nominate as a candidate for ORDINARY MEMBERSHIP/OVERSEAS/ ASSOCIATE/TRAINEE MEMBERSHIP

....

1. (Signed) ....
(NAME IN BLOCK LETTERS)

Address ....
BLOCK LETTERS

2.(Signed) ....
(NAME IN BLOCK LETTERS)

Address ....
BLOCK LETTERS

*** See the reverse of this page for details of membership categories.**
† One sponsor must be an Ordinary Member of the Association.

THIS PAGE CONCERNS YOU IF YOU ARE A MEDICALLY QUALIFIED ANAESTHETIST IN GREAT BRITAIN AND IRELAND, OVERSEAS OR IN TRAINING AND ARE NOT YET A MEMBER OF THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND OR IF YOU ARE A MEMBER OF ANOTHER PROFESSION WHO PRACTISES IN ANAESTHESIA

AND YOU WISH TO APPLY FOR ASSOCIATE MEMBERSHIP

Ordinary Membership (*United Kingdom and Ireland only*)

Voting membership of the Association (the only effective body representing anaesthetists' interests in non-academic matters).

The right of attendance at the Annual General and Scientific Meetings and all other meetings of the Association of Anaesthetists.

Overseas and Associate Membership

The right of attendance at the Annual Scientific Meeting and other meetings of the Association.

Trainee Membership (*United Kingdom and Ireland only*)

Voting membership of the Association.

Representation on the Council of the Association. The Chairman and Secretary of the Trainee Group sit on Council as voting members.

Attendance at the Annual Scientic Meeting of the Association and at the special Annual Scientific Meeting of the Anaesthetists in Training, at which Trainee Members of the Association are given preference.

Membership Fees (inclusive of the journal *Anaesthesia)*

Ordinary Members: Subscription £110 (Husband and wife £80 each)

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Trainee Members Subscription: £55 (£75 after 3 years if still in training)

Retired Members: who receive Anaesthesia £15 (there is no subscription for those who do not).

How to apply for membership

Fill in the application form on the other side of this page.

Have it countersigned by two members or the Association, one of whom must be an Ordinary Member.

Tear out the page and send it to the address indicated overleaf.

Do not send money with your application

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Manuscripts will be reviewed for possible publication on the understanding that they are being submitted to one journal at a time and have not been published, simultaneously submitted, or already accepted for publication elsewhere. This does not preclude consideration of a manuscript that has been rejected by another journal or of a complete report that follows publication of preliminary findings elsewhere, usually in the form of an abstract. Investigations performed on man must conform to appropriate ethical standards including voluntary, informed consent and acceptance by an ethics committee. Articles accepted become copyright of *Anaesthesia.*

Contributors are requested to submit two copies of manuscripts. They are also advised to retain a third copy as the Editors cannot accept responsibility for the loss of manuscripts in the post. The covering letter should be signed personally by all the authors. Articles should be forwarded to:

Dr M. Morgan, Department of Anaesthetics, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS, UK.

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Type manuscripts on white bond paper, 20.3 × 26.7 cm or 21.6 × 27.9 cm (8 × 10½ in. or 8½ × 11 in.) or ISO A4 (212 × 297 mm) with margins of at least 2.5 cm (1 in.). Use double, and preferably triple, spacing throughout, including the references. Please do not use a dot matrix printer, particularly one with poor quality descenders or ascenders. Unseparated, fan-folded manuscripts may be returned to the author. *The manuscript* should consist of the following sections in this order each beginning on a new page: *title page, summary* and *key words, text, acknowledgements, references, individual tables,* and *legends for figures.*

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SUMMARY AND KEY WORDS

Start a new sheet

The second page should carry a summary of not more than 150 words. The summary should state the purpose of the study or investigation, basic procedures, main findings and their statistical significance, and the principal conclusions (it should not state that the results are discussed).

Do not use abbreviations except for units of measurement (e.g. mg, cm, etc.).

Key (indexing) words. Below the abstract, provide and identify as such, three to 10 key words or short phrases that will assist indexers. Use terms from the Medical Subject Headings list from *Index Medicus.* The Editor may modify these at proof stage to conform with agreed practice of certain other anaesthetic journals in the English language.

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Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by arabic numerals. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. Use double or treble spaced typing.

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(continued overleaf)

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Examples of correct form of references

Note: first and last pages in all references.

JOURNAL

Standard journal article—(List all authors)

Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294:** 687–90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:** 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

Osler AG. Complement: mechanisms and functions. New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. AMA drug evaluations, 3rd edn. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

Rhodes AJ, Van Rooven CE, *comps. Textbook of virology: for students and practitioners of medicine and other health sciences,* 5th edn. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

Weinstein L. Swartz MN. Pathogenic properties of invading miro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease.* Philadelphia: W.B. Saunders, 1974: 457–72

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968—June 1969. Rockville, MD: National Center for Health Statistics, 1972. (*Vital and health statistics, Series* **10:** Data from the National Health Survey. No. 69) [DHEW publication No. (HSM) 72–1036].

OTHER ARTICLES

Newspaper article

Shaffer RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

Roueche B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

TABLES

Do not include tables in the text. Start a new sheet for each table and space the material adequately. The author(s) name(s) should appear in the top right-hand corner.

Indicate the approximate position of each table in relation to the subject matter of the text in the left-hand margin of the appropriate page on the manuscript. Do not submit tables as photographs. Number tables consecutively with arabic numerals. Supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes. Explain in footnotes all non-standard abbreviations that are used in each table. For footnotes, use the following symbols in this sequence: *, †, ‡, §, ||, ¶, **, ††, etc. Identify statistical measures of variations such as SD and SEM. *Legends for tables* should appear on the face of the table.

Cite each table in the text in consecutive order and mark the approximate position of the table in the left-hand margin of the text.

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All sources of identification of patients must be removed.

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Type legends for illustrations double spaced with arabic numerals corresponding to the illustrations. When symbols, arrows, numbers or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

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Statistics and measurements should be given in figures except that numerals one to nine should be in words if not followed by a measurement symbol (e.g. 'two patients' but 2.0 mg'). The *Système International* (SI) will usually be used except that vascular pressures will be recorded in mmHg and cmH_2O. Imperial measurements will not be used except in an historic context. The 24 hour clock will be used.

Contributors are advised to study the SI *Conversion Tables* provided in the January 1978 issue of *Anaesthesia, Units, Symbols and Abbreviations* (*A Guide for Biological and Medical Editors and Authors*) published by the Royal Society of Medicine, London W1M 8AE, and *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5).

The statistical tests used in the report should be stated clearly. Results should include 95% confidence limits for the main findings and probability estimates.

LETTERS FOR PUBLICATION

Should be addressed to *Dr M. Morgan,* Department of Anaesthetics, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS, UK.

Letters should be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters above. The degrees and diplomas of each author must be given in a covering letter which must be signed personally by all the authors.

Correspondence presented in any other style or format may be subject to considerable delay and may be returned to the author for revision.

The editors regret that failure to comply with the above requirements may result in a delay in publication of accepted papers.

REVIEW JOURNALS

This journal is covered by *Current Contents, ASCA,* the *Science Citation Index and Index Medicus.*

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